ACTA RADIOLOGICA
EDITA PER SOCIETATES RADIOLOGICAS DANIÆ, FENNIÆ,
HELVETIÆ, HOLLANDIÆ, NORVEGIÆ ET SUECIÆ

VOL. XXX FASC. I—II 31 : VIII 1948 N:o 173—174

ROENTGEN EXAMINATIONS OF THE SOFT TISSUE IN ACUTE THROMBOSIS[1]

by

J. Frimann-Dahl

In acute thrombosis venography has hitherto been the most usual method of roentgen examination. BAUER and HELLSTEN especially have in a series of articles demonstrated that venography can reveal an acute thrombosis in an early stage. A fresh thrombosis shows at first irregular defects and clearings in the contrast-shadow and discontinuities of the venous net-work. Later on a complete obstruction to the passage through the deep veins will develop, while at the same time the saphenous vein little by little increases in breadth and carries the main part of the blood stream.

By means of venography it has been proved that most cases of acute thrombosis have their origin in the deep venous trunks of the calf (BAUER). By this method also the various pressure conditions in this region, which are an aetiological factor, may be studied (FRIMANN-DAHL). The method is easy to perform, even in patients in so bad a condition that removal from bed is impossible. Generally the vein is punctured percutaneously and the contrast medium injected in the course of about 30 sec. Sometimes the vein must be exposed; and great care should always be taken to prevent the contrast coming outside the vessel, otherwise local necrosis may occur. The interpretation of the films may be difficult, and great experience is required to rely completely on the findings.

Many surgeons claim today that all patients in whom a thrombosis is suspected, should be examined by venography. This is important because the treatment with anticoagulants must be begun as early as possible. Generally, however, the use of venography in acute thrombosis is limited, mainly because the method is expensive and the clinical diagnosis in most cases is fairly definite.

[1] Submitted for publication, Febr. 23, 1948.

From the Roentgen Department of Oslo Municipal Hospital Ullevål, Norway (Chief: J. FRIMANN-DAHL, M. D.).

In recent years we have tried a second method to demonstrate acute thrombosis of the lower extremities, namely the soft tissue examination. Films of the soft tissues have been investigated long ago. Thus CARTY in 1936 studied the contours of the extremities. Normally the subcutis is seen as a clear zone of varied size depending on the amount of subcutaneous fat. Superficially this clear zone is definitely outlined by the so-called cutis-line corresponding to the skin. The edge of the muscular tissue is also well defined towards the subcutaneous fat. Normally in the subcutis some small bands due to the veins are seen, and probably also some nerves and lymphatic vessels are visible. Some fine stripes corresponding to the fasciae are sometimes present.

In 1944 FRANTZELL published an article on soft tissue examinations in various types of edema. His investigations are founded on the work of LAURELL concerning the roentgen appearences of the soft tissues dating back as far as 1920. The first observations LAURELL made were in osteomyelitis in children, and later also the changes in the flanks in inflammatory conditions were scrutinized. These observations were continued by SKARBY in a work on para- and perinephritis. It is probable that the changes of the soft tissue in thrombosis in a similar way are caused by hyperemia, stasis in the vessels and edema.

After injections of fluid subcutaneously, FRANTZELL could demonstrate that most of the abnormal markings in the subcutis were due to retention of fluid in the tissue: *subcutaneous edema.* These findings are, as it will be understood, therefore mainly symptomatic, but where the changes are seen on the one side only, and where an acute thrombosis is suspected, the diagnosis is fairly probable.

FRANTZELL gives the following three points typical for the edema:

1. Thickening of the cutis-line.
2. Increased breadth of the subcutaneous fatty layer.
3. Abnormal net-worklike designs in the subcutis.

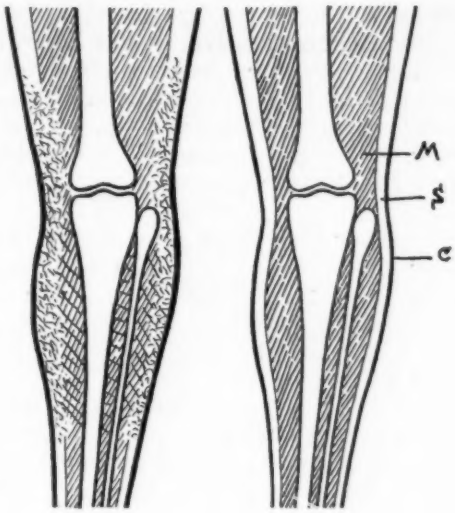
To these can be added as typical for thrombosis:

4. Increased density of the muscular shadow and blurring of the border of the muscle mass adjacent to the subcutaneous fat. (Fig. 1.)

During revision we like to add a 5th sign: Dilatation of collaterals and broadening of the saphenous vein (without injection of any contrast medium).

In his work FRANTZELL has mentioned the possibility of diagnosing acute thrombosis by means of this method. A negative finding should be equally valuable to show that no thrombosis is present. He further points out that the thrombotic edema has a characteristic localisation, but he does not publish any material.

At Ullevaal Roentgen Department 34 patients with an acute thrombosis were examined in the course of the last years. In the present contribution the results of these investigations will be dealt with.



A. B.

Fig. 1. A. Diagram to show the changes of the soft tissues in acute thrombosis. B. Normal. M = Muscle, S = Subcutis, C = Cutis.

Technique

The method is as mentioned easy to perform. The roentgenograms may very well be taken when the patient is lying in bed, though better pictures are obtained if the patient can be placed on a Bucky-table. The casette is placed right under the calves, and the exposure may if desired be made with a mobile unit. Thus transport of the patient to the roentgen department is not absolutely necessary, and the examination can be made in the ward. The main point is not to have the films overexposed. The skin contours of the limb must be clearly outlined. Normally 40—50 kv. and 100 M. A. are required, time of exposure $^1/_2$ sec., target—film distance 90—100 cm. Care must also be taken to control the development of the film and keep the darkening strictly within limits. The subcutaneous layer, which is the most translucent part of the extremity, must have a certain clarity on the film. A casette size 30 × 40 cm is convenient, and should be placed so that the lower part of the thigh is included. When occasionally a thrombosis in the upper part of the thigh is suspected, a film should be taken right up to the groin. The normal side is always photographed for comparison, and both extremities exposed simultaneously. When the extremities are rather heavy as in adiposity, a 40×50 cm casette is preferable. It is always important that the lateral border

is not covered or cut off. The best pictures are obtained when the patient is lying on a Bucky-table and a movable grid is used.

In ordinary cases the pathological changes in the soft tissue are more distinctly visible when the panniculus adiposus is abundant. Thus the diagnosis is more easy to make in women with a broad subcutaneous clear zone than in men where the muscle mass is more prominent. In some of these cases the only sign was a widening of the extremity (compared to the other side).

The Material

The above mentioned main symptoms correspond closely to our findings. The investigations have been undertaken as early as possible and in many cases within the first or second day. 34 cases had clinical signs of thrombosis and 30 of these showed positive roentgenological changes. (Fig. 2.) In order to verify the findings and the thrombosis, a venography was made simultaneously with the soft tissue picture in 13 cases. All of the these showed positive changes either as defects in the venous contrast or a total hindrance of the passage through the deep venous trunk.

In 4 cases the clinical diagnosis was certain, while the roentgen examination was almost negative. In two cases the diagnosis was uncertain both clinically and roentgenologically, and finally the radiographs showed positive signs in 3 cases where the clinical symptoms initially were negative. It therefore proves that the new method may give symptoms before it is possible to diagnose the thrombosis clinically.

In a great number of cases the roentgen findings were negative and this was later proved to be correct by the subsequent clinical course.

At an early stage the pathological designs in the soft tissues may be badly visualized. The findings are deemed to be most pronounced on the lateral border at a level corresponding to the calf. They successively spread towards the thigh. When the edema can be demonstrated clinically it is also easy to show on the films of the soft tissue.

A question arises namely whether it is possible to point out the thrombosis earlier by means of venography than by the new method. In certain patients that no doubt is the case. In a man's leg, as previously mentioned, the subcutaneous fat may be so limited that the designs due to thrombosis are too scanty for a definite diagnosis. In some such cases a venography has proved thrombosis. 3 cases of that kind have been examined by us. In all the thrombotic masses were adherent to the walls of veins, and the occlusion of the vessels was not complete. Perhaps that is an explanation of the poor findings of the soft tissue pictures.

Studies of venographic findings on survey films of the soft tissue have proved that an acute thrombosis may give a marked dilatation of the

Fig. 2. Acute thrombosis of the left leg 1 day after onset of symptoms. Network-like markings in the subcutis present both med. and laterally. This film has been copied by a special method, the so called »tone-separation». Otherwise the details in the soft tissue are very difficult to reproduce.

subcutaneous vessels and hyperemia. The network-like designs in the subcutis are thus accordingly not only due to edema and fluid, but are also largely caused by the dilated vessels in many cases. (Fig. 3.)

On account of these findings we are more inclined to call the pathological changes *»thrombosis designs»* than »edema designs» or possibly bet-

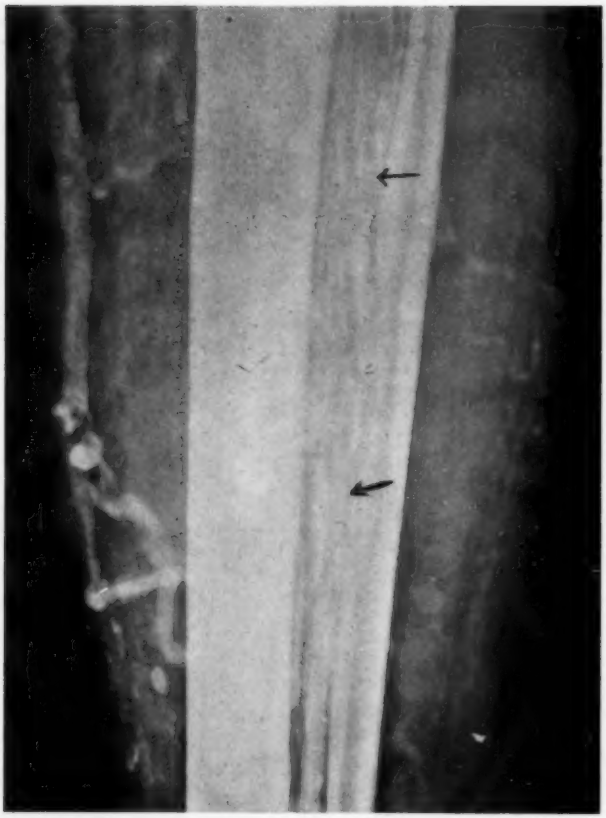


Fig. 3. Simultaneously venography and soft tissue picture in acute thrombosis. Dilated vessels and edema in subcutis. Arrows indicate thrombosis masses.

ter still: *»vessel-edema design»*. From the experiences gained it may be stated that the roentgen examinations of the soft tissue provide a new method for the diagnosis of acute thrombosis in the extremities. If the findings are negative the first time, a re-examination may easily be performed. One or two days later the characteristic changes may possibly appear.

Differential Diagnosis

Naturally it is an important question whether other diseases give changes on the roentgenograms similar to those of acute thrombosis.

We have mentioned already that the findings are not specific, but due to edema and hyperemia. Then by what is the situation in cardiac or general edema to be differentiated? In these the changes appear initially in the distal part of the legs and later are seen *bilaterally* below the knee-joint.

In acute spontaneous thrombosis the pathological changes are found on one side only, and are generally first seen in the calf. In the course of some days they increase and may spread up towards the groin. In the differential diagnosis the edema caused by *fractures* also requires consideration. A fracture of the upper part of the leg is nearly always attended by edema and we also know that thromboses are a frequent complication. In our material there are 4 such cases where the soft-tissue pictures showed abnormal »edema designs». The diagnosis could not be made on the basis of these alone, and a venography had to be performed. In two cases the injection of contrast revealed trombotic masses in the deep veins. The other cases showed no signs of thrombosis. So it was proved that when a differentiation between thrombosis or fracture edema is to be made, a venography is conclusive. A *hematoma* due to a fracture may also give changes suggestive of a thrombosis, and here again venography is decisive. The same situation arises when edema is found after the removal of a plaster-cast.

In this connection it can be mentioned that BAUER has found a surprisingly large number of thromboses in cases of fractures in the proximal part of the leg. So when these cases are to be investigated, the soft-tissue pictures can not give a definite answer which is provided here by a venography. A differential point is that the fracture edema is localized on both sides of the fracture and is not apt to descend. Another and more occasional finding is similar changes due to *phlegmonous inflammation* in the leg. Then also the soft-tissue changes can suggest a thrombosis, but here the clinical symptoms are so prominent that no real difficulties arise.

As already mentioned *osteomyelitis* may also give edema-like designs. This occurs mainly in children and may be visible before the changes in the bone. So in adults this cause will be relatively uncommon, but it must be kept in mind.

Finally the question arises of *how long* a thrombotic edema persists, and how long after the onset the symptoms may be demonstrated. This can for the present not be exactly answered. Clinical experience shows that the findings are most variable and the roentgenological changes reflect this. When Heparin treatment is instituted, the findings will disappear very soon, and had in one case completely vanished after 5 days. Here venography showed thrombotic masses adherent to the wall of the veins, so that the conditions for a complete occlusion were not present. In another case with total blockage the changes persisted for at least one month.

Consequently it is possible that the soft-tissue examination is valuable not only in the acute stage but also can be used as a control for the effect of various sorts of treatment. Generally speaking it is a great advantage that the soft-tissue examination can be repeated as often as wanted.

SUMMARY

Roentgen examination of the soft tissues may show edema and hyperemia of the extremities in acute thrombosis. At an early stage the changes may be scanty, but may also, and contrary to this, be present when the clinical signs are uncertain. The findings are most easily distinguished when the subcutaneous fat is abundant, and more easily visualized in women than in men. This method is an aid to the clinical diagnosis in both positive and negative directions. Venography may give the necessary complementary evidence for the diagnosis.

ZUSAMMENFASSUNG

Ödem und Hyperämie der Extremitäten bei akutem Thrombosis können durch Röntgenuntersuchung der Weichteile nachgewiesen werden. In einem frühen Stadium sind die Veränderungen oft unbedeutend, können doch sichtbar sein auch in Fällen, wo die klinische Diagnose unsicher ist. Sie treten am besten hervor, wenn die subcutane Fettschicht sehr entwickelt ist und besser bei Frauen als bei Männern. Diese Methode ist von Wert für die klinische Diagnose sowohl in positiver als auch in negativer Richtung. Durch komplettierende Venographie kann die Diagnose festgestellt werden.

RÉSUMÉ

La radiographie des parties molles peut mettre en évidence l'œdème et l'hyperémie au niveau des jambes de malades atteints de thrombose. A un stade précoce les altérations sont souvent peu manifestes, mais peuvent aussi être nettes alors que le diagnostic clinique est incertain. Elles sont plus faciles à voir là où la couche adipeuse souscutanée est fortement développée. Elles sont plus nettes chez les femmes que chez les hommes. Cette méthode peut être précieuse dans le sens positif comme dans le sens négatif. La veinographie peut apporter le complément nécessaire au diagnostic.

REFERENCES

1. Bauer, G.: A Roentgenological and Clinical Study of the Sequels of Thrombosis. Acta Chir. Scand. Suppl. 74. 1942.
2. Carty, I.: Soft tissue Roentgenography. Amer. J. of Roentgenol. Bd. 35. 1936.
3. Frantzell, A.: Röntgenologische Weichteilstudien von Cutis und Subcutis. Acta Radiol. 25. 460. 1944.
4. Frimann-Dahl, J.: On Venography of the Lower Extremities. Acta Radiol. 28. 199. 1947.
5. Hellsten, W.: Phlebographic Studies. Acta Chir. Scand. Suppl. 73. 1942.
6. Laurell, H.: Ein Beitrag zur Röntgendiagnostik der Peri- und Paranephritis. Uppsala Läk.förenings förhandl. 1921.
7. Skarby, H. G.: Beiträge zur Diagnostik der Paranephritiden. Acta Rad. Suppl. LXII. 1946.

FROM THE DANISH CANCER REGISTRY UNDER THE NATIONAL ANTI-CANCER LEAGUE, COPENHAGEN, DENMARK (DIRECTOR: JOHANNES CLEMMESEN, M. D.)

THE AGE DISTRIBUTION OF MALIGNANT DISEASES IN DENMARK 1942—44[1]

by

Johannes Clemmesen, M. D. and *Thøger Busk*, Lic. act.

In a previous paper from the present institute (Acta Rad., Vol. 29, pag. 321) the absolute figures for cases of various malignant diseases in Denmark known to The Cancer Registry were given for the years 1942—44, together with the percentage of cases admitted in hospital or verified by histological or post mortem examination. The paper also contained a description of the organisation of the registry together with a survey of its various activities.

It was, however, pointed out that the steep increase of cancer incidence with age makes it very important that the composition of the material should be known for all classes of age, and it is the aim of the present paper to give such information on forms of cancer sufficiently frequent to permit the construction of curves on their distribution by age based on quinquennial classes.

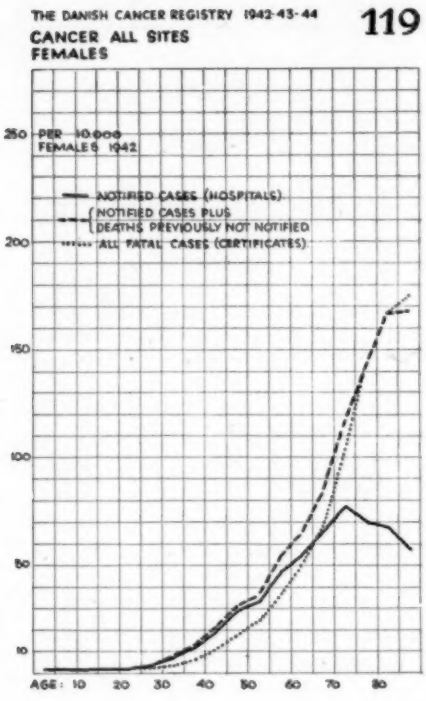
As previously mentioned the quality of the material will vary between cancers of different site with the percentage of hospital admittance. But also the application of hospital examination and treatment varies with age, and so each diagram contains three curves which for all but practical reasons should have formed each its separate diagram.

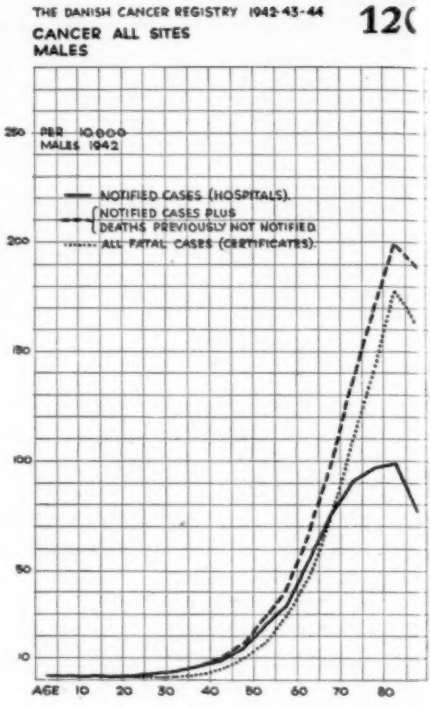
1. The curve given in full shows hospital cases according to age when first seen in hospital.

2. The dotted line gives the fatal cases reported among the entire material without regard to hospital treatment, and distributed according to age at death.

The diagnoses of these cases have been sorted out in the Cancer Registry and consequently not infrequently corrected according to clinical and autopsy findings so that differences from the official material, based solely on the diagnoses of death certificates, may occur. Other

[1] Submitted for publication, Febr. 13, 1948.



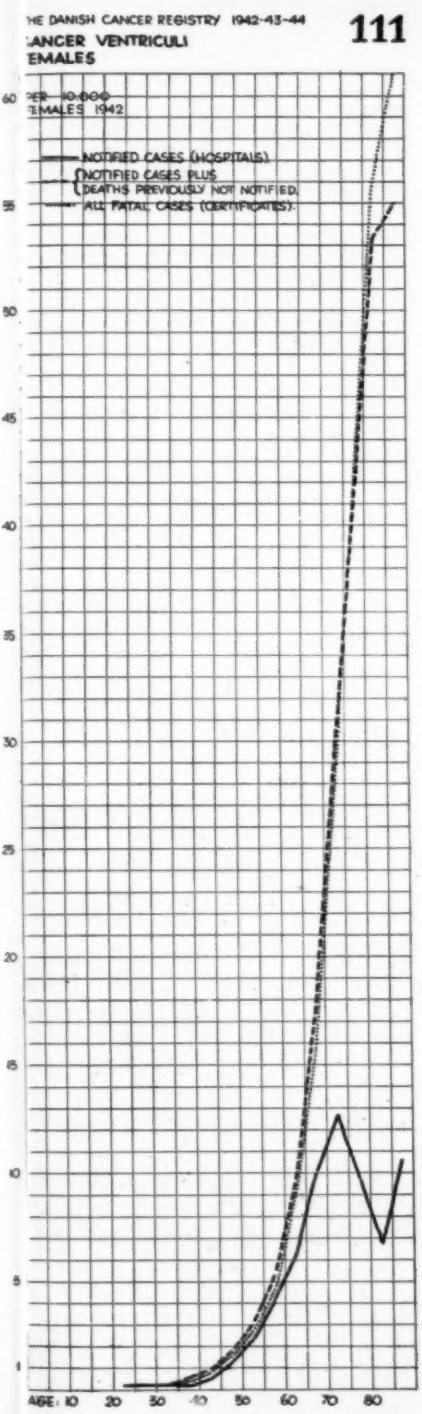


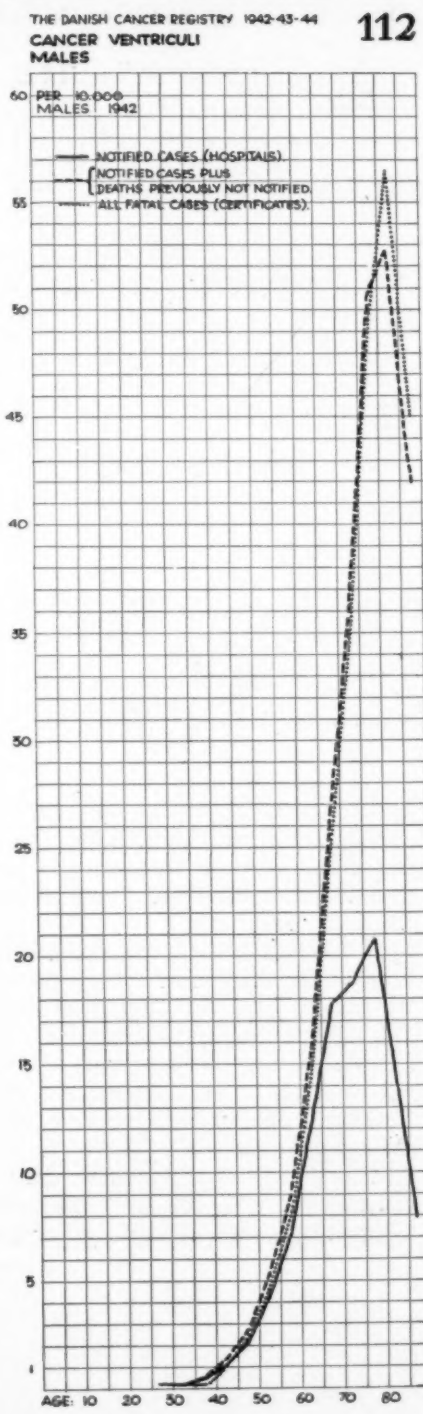
and heavier divergencies will be due to the different limitation of the material, which here covers all deaths among cases reported, whether ascribed to cancer or not.

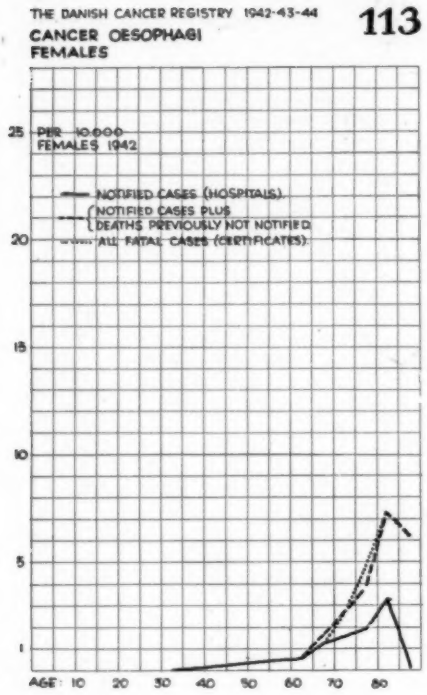
3. The dashed curve represents the total material of the Cancer Registry, consisting mainly of hospital cases, distributed according to age when first seen in any hospital, and partially of fatal cases known to the Registry solely from death certificates. Such cases must naturally be grouped according to age at death, as no other well-defined point of time will be available.

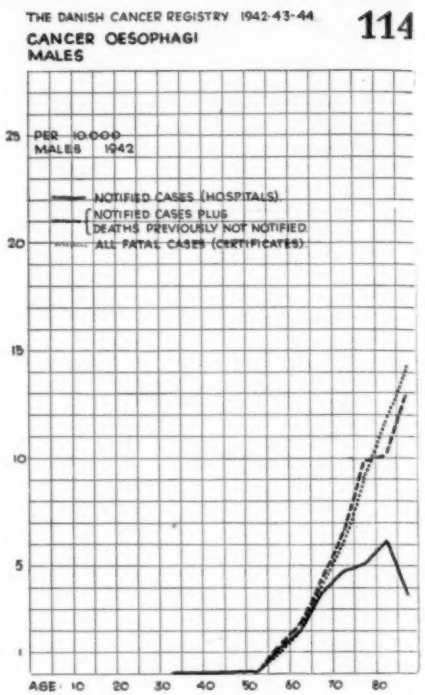
This naturally qualifies the value of the curve for research purposes, so that it should be taken mainly as representing the age distribution of a cancer registry material.

As it will be seen from the diagrams, the accordance between the three curves is usually satisfactory for the younger age classes. However, the diagram on breast cancer (52) clearly illustrates the consequences of the construction of the diagrams: In this case where treatment is rather


HE DANISH CANCER REGISTRY 1942-43-44
111
ANCER VENTRICULI
EMALES
PER 10.000
EMALES 1942
NOTIFIED CASES (HOSPITALS)
NOTIFIED CASES PLUS
DEATHS PREVIOUSLY NOT NOTIFIED.
ALL FATAL CASES (CERTIFICATES).
60
55
50
45
40
35
30
25
20
15
10
5
1
AGE: 10 20 30 40 50 60 70 80


THE DANISH CANCER REGISTRY 1942-43-44
112
CANCER VENTRICULI
MALES
PER 10.000
MALES 1942
NOTIFIED CASES (HOSPITALS)
NOTIFIED CASES PLUS
DEATHS PREVIOUSLY NOT NOTIFIED.
ALL FATAL CASES (CERTIFICATES).
60
55
50
45
40
35
30
25
20
15
10
5
1
AGE: 10 20 30 40 50 60 70 80

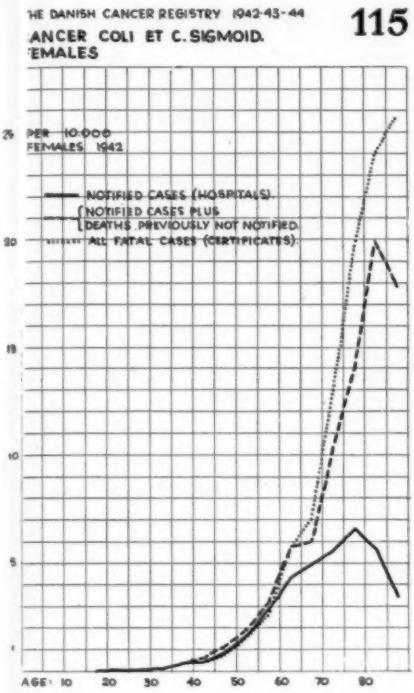


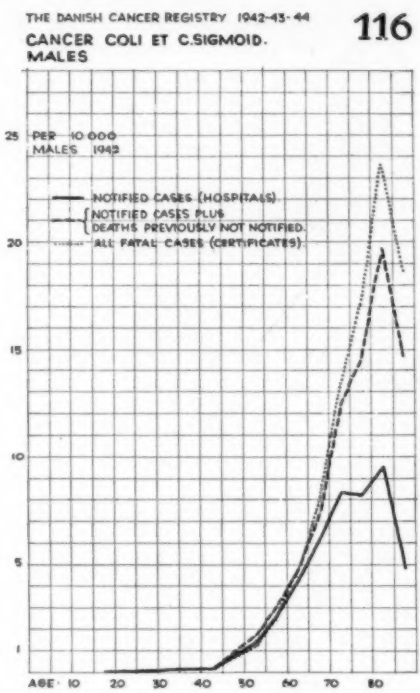


effective, the curve for hospital cases runs at a higher level than the mortality curve. This difference, however, will not only be due to cases cured but also to the average period between admittance in hospital and death, because the two curves are constructed according to ages of different definition.

Another feature, not immediately intelligible, is the occasional higher level of the dotted mortality curve over the dashed curve representing the sum of pure mortality (*i. e.* death certificate) cases and hospital cases. This phenomenon is mainly seen in the classes of high age. It is due to the fact that a hospital case with a fatal course will be grouped according to age at death when contributing to the dotted mortality curve, but according to age when first seen in hospital when the other two curves are worked out.

Thus, the mortality curve may at a certain age represent a number of cases which in the two other curves of the same diagram have been referred to a class of slightly lower age. As the age groups comprise five

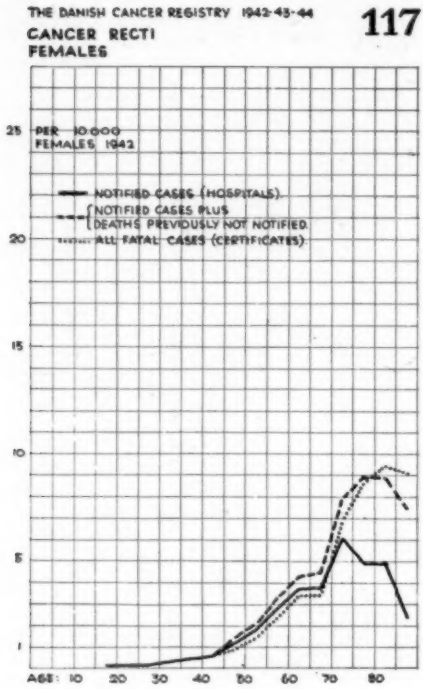


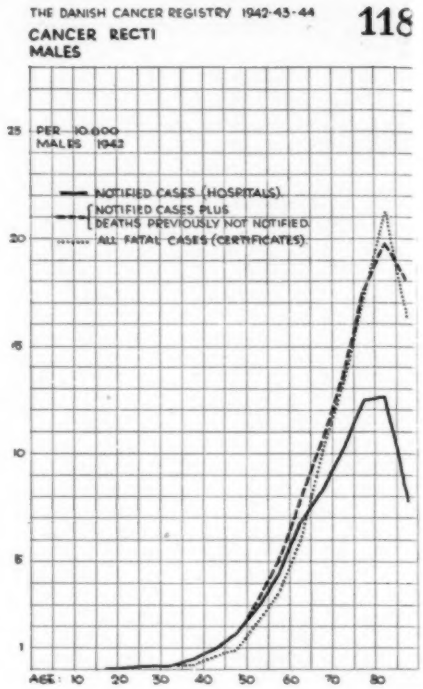


years each, it will be understandable that the consequences hereof are rather limited, but considerable reservation should be taken at any direct comparison between the three curves of the same diagram. It will be understood that difficulties of this kind — unveiled or not — will be fundamental in all cancer statistics based on cases both from hospitals and from general practice, but fortunately they are most pronounced in the older age classes where the number of hospital cases is fairly small.

It will be noticed that all diagrams have been worked out based on quinquennial age groups and with the same vertical scale, so that the shapes of the curves are directly comparable even if their magnification is different.

With regard to the different forms of cancer, it should be noticed that cervical and fundus cancer of the uterus are combined in the same diagram (51). They are worked out without special curves for hospital cases because these make out respectively 98 and 92 per cent of the total so that special curves would only serve to confuse the diagram.



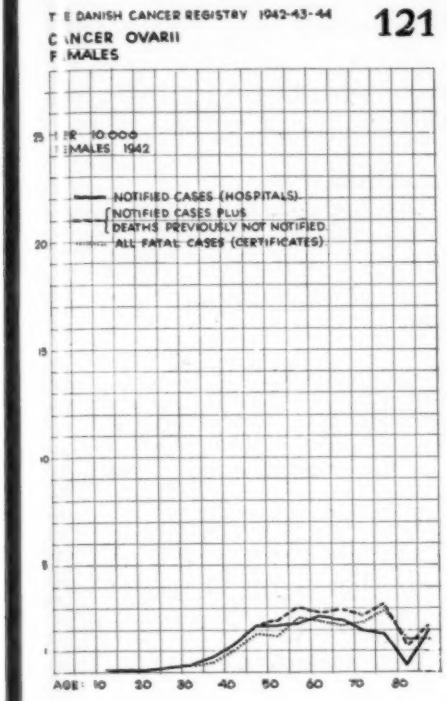


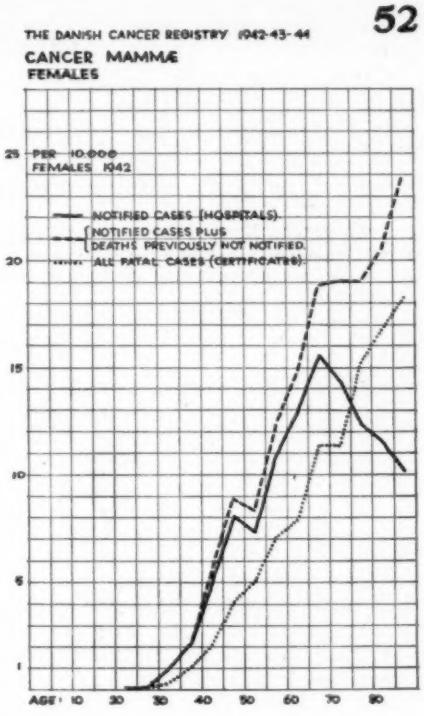
Similar views have been applied to the group of unspecified cases, which for 87 per cent is based on death certificates. The diagram explains the increase in the proportion of fundus cancers found in countries with ageing populations and serves as a warning against unspecified statistics on uterine cancer.

Breast cancer (52) displays an interesting irregularity of the curves about the 55 year. The fall in incidence about that age is statistically significant for the three years in question but seems less pronounced for the following years (BUSK & CLEMMESEN).

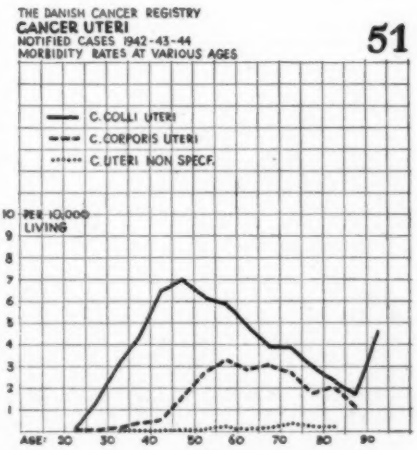
It would not seem unreasonable to connect this irregularity with climacterial phenomena but at the moment no final explanation can be given (CLEMMESEN 1948). The slight fall observed about the same age in the curve for female cancers of all sites, may be ascribed to the movements in breast cancer, but also the uterine cancers may be of influence here.

The material given in this and the preceeding article is to some extent suffering from representing the first three years of the Danish Cancer





Registry, as according to American experience the material will show a slight improvement through the first few years of registration. Nevertheless, we feel justified in giving our material as detailed as possible; our justification for this is firstly that Denmark offers excellent conditions for detailed analysis of the function of a registration system, and secondly our obligation to submit the material for the early use of the numerous doctors whose clinical work and interested participation in our schemes have created the conditions for our work.



SUMMARY

Curves on the age distribution of various forms of cancer notified to the Danisl Cancer Registry 1942—44 are given and commented upon, illustrating the difference between mortality and morbidity statistics on cancer.

ZUSAMMENFASSUNG

Es werden Kurven gebracht und besprochen über die Altersverteilung verschiedener Formen von im Dänischen Krebsverzeichnis 1942—44 vorliegendem Krebs, wodurch die Unterschiede zwischen Mortalitäts- und Morbiditätsstatistiken bei Krebs veranschaulicht werden.

RÉSUMÉ

Reproduction, avec commentaires, de courbes indiquant la répartition par classes d'âge des diverses formes de cancers annoncés au Bureau Danois de Statistique du Cancer de 1942 à 1944; ces courbes illustrent les différences entre les statistiques de mortalité et de morbidité cancéreuses.

LITERATURE

Busk, Th. and Clemmesen, J.: The frequencies of left- and rightsided breast cancer. Brit. Journ. Cancer. Vol. 1, pag. 345, 1947.

Clemmesen, J.: Breast Cancer. Statistical Results. Brit. Journ. Radiol. being printed.

Clemmesen, J. and Busk, Th.: The Incidence of malignant Diseases in Denmark 1942—44. Acta Rad. Vol. 29, pag. 321, 1948.

FROM THE CENTRAL TUBERCULOSIS-DISPENSARY IN COPENHAGEN, DENMARK
(CHIEF: KNUD WINGE, M. D. — ROENTGENOLOGIST: NIELS CHRISTIANSEN)

ON THE DIFFERENT FORMS OF PHTHISIOGENOUS INFILTRATES AND THE DEVELOPMENT OF PHTHISIS[1]

by

Niels Christiansen

I. Introduction

The question of how pulmonary tuberculosis starts has occupied scientific research long before ROBERT KOCH in 1882 discovered the tubercle bacillus. Even LAËNNEC who, in the beginning of the last century, was the first to acknowledge the tuberculous disease as a nosological unity, maintained as a result of clinical and patho-anatomical observations that pulmonary tuberculosis started in the apices and thence spread downwards. This conception also remained after the discovery of the bacillus, and from the beginning of this century to the middle of the twenties the general view on the origin of phthisis was — as is known — that most people were infected in their childhood either by patients suffering from phthisis or by drinking infected milk. The children who outlived the primary infection kept the bacilli encysted in the bronchial or mesenteric glands, and these foci might later on give haematogenous seed to the lungs of the adults. As a rule the process would begin as an apical catarrh, from there spreading slowly apico-caudally. The primary infections in adults were considered very rare, which they probably also were at that time.

BEHRING's demonstration of the great frequency of intestinal infection in children (1903), PIRQUET's introduction of the allergic theory (1906) and the methods of intra-dermal tuberculin reaction made shortly afterwards — through which it was proved that up to 95 % of schoolchildren were reacters — only confirmed this point of view. The works of RANKE and COHN on the tuberculous primary complex (1911—12) and RANKE's »Stage-Doctrine» — the primary complex, the dissemina-

[1] Submitted for publication, March 30, 1948.

tion and the stage of localisation — contained nothing which might cause any change in this conception.

But parallel to the scientific progress the campaign against tuberculosis now commenced in earnest. Still more sanatoria and dispensaries were founded, the therapy became more active and bovine tuberculosis was combated. At the same time the social and hygienic conditions improved. The effect of all this was that epidemiologic conditions gradually altered. Fewer and fewer were infected in childhood and in consequence thereof the percentage of reacters among young people diminished. Thus primary infection in adults became more frequent than before.

In this period a rapid development of roentgen technique also took place. Owing to better roentgen tubes and more sensitive films the time of exposure was considerably reduced. The photos of the lung were highly improved; even small pathological changes in the parenchyma now could be observed.

II. The »Doctrine of Frühinfiltrat»

At the close of the two first decades of this century all conditions were thus present for finding and observing the first roentgenological manifestations of the pulmonary tuberculosis, and this actually took place.

In 1922 ASSMANN was the first to demonstrate a form of isolated tuberculous focus in adults. It was by SIMON named »Frühinfiltrat», and in the succeeding years BRAEUNING & REDEKER worked out the socalled »Doctrine of Frühinfiltrat».

BRAEUNING & REDEKER themselves admit that the »Frühinfiltrat» is neither a genetic nor a patho-anatomical unity, but a »clinical-roentgenological term». It is defined as a limited perifocal reaction surrounding a fresh tubercular focus in a lung not phthisic before. Although in many cases it was accompanied by a hilar enlargement it was not to be identified with a primary infiltrate as it belonged to RANKE's 3rd phase, the stage of localisation. The origin might be caused either through superinfection or haematogenously from old glandular foci. It was mostly localised in the infraclavicular region while apices were free. It was chiefly to be found in young people and as a rule caused no or slight subjective symptoms, and — what was even more important — it could only be demonstrated roentgenologically.

They concluded that the old theory on the origin of pulmonary tuberculosis in apices was wrong. In their opinion most phthisis originated from an infraclavicular »Frühinfiltrat» and the spread to a florid phthisis did not occur slowly apico-caudally, but in periodical propagations, »Schube».

In later works the two authors and their collaborators further develop the »Doctrine of Frühinfiltrat» adding other haematogenous forms of in

filtrates to it, of which the most important are the secondary haematogenous spread, »Spätstreuung», and the so-called »Interval forms», *i. e.* infiltrate-residues, which at times may develop to »Nachschub»-infiltrates (reactivity-infiltrates).

At its inception the »Doctrine of Frühinfiltrat» attracted justified attention all over the world, and although on essential points the doctrine later on proved to be wrong — to which I shall return later — it soon led to the important consequence that it caused a change in the principles of combating tuberculosis. The roentgen examination was from now on considered indispensable, and one comprehended the necessity of extending the investigation to persons who did not show any symptoms of tuberculosis but were exposed to infection, first within the tuberculous milieu and later to larger groups of persons who were estimated especially exposed such as nurses, students, etc. The result was that the early stages of pulmonary tuberculosis now were observed more often than before, and this again had a stimulating influence on the scientific interest in the problem: *tuberculosis incipiens*.

III. Recent Scandinavian Researches

In the years from the middle of the twenties up till now a series of valuable works on this subject have been published. As comparative clinical and patho-anatomical investigations — for well known reasons — could not be carried out, researches had to be based upon serial investigations with frequently repeated roentgen examinations, tuberculin tests and — during the later years — also by energetic bacillus investigations. Here only a few of the most important works by Scandinavian authors, foremost in this respect, shall be mentioned.

Heimbeck (1933—36) and Sheel (1937) found in invertors (*i. e.* patients who have changed from tuberculin-negative to positive) infiltrates which had a remarkable resemblance with the »Frühinfiltrat», but none the less had to be considered primary infiltrates.

Based on minute and systematic serial examinations of students and nurses during the years 1930—37 Malmros & Hedvall (1938) demonstrated that pulmonary tuberculosis in their invertors did not originate from solitary infraclavicular infiltrates of the type »Frühinfiltrat», nor from primary foci, but as a rule from small or somewhat larger, irregular, cloudy, usually multiple spots, »subprimary initial foci», often situated in the supraclavicular region or the first intercostal space, or in both these regions at the same time. They arose about 12—14 months after the primary infection.

Frostad (1944) has studied the development of pulmonary tuberculosis in 158 patients with apparent primary affections. In the majority of

his cases the phthisis developed from rather large infraclavicular infiltrates which in several cases seemed to be primary foci. Some of these instantly showed a tendency towards an acute rapid development, while other cases showed that the primary focus after having undergone regression was able to become active again and form the starting-point for phthisis; the reactivity might occur as late as $2^1/_2$ years after the primary infection. The conclusion that pulmonary tuberculosis often develops directly from a primary infiltrate was to a certain extent contrary to former opinions. However, FROSTAD maintained that many of the infiltrates which previously were considered »Frühinfiltrat» arising secondarily, in reality had been primary foci, pointing out, that BRAEUNING & REDEKER as a rule had no knowledge of their patients' earlier tuberculin tests. As it concerned adults, they *a priori* assumed that the patients long since had turned tuberculin-positive, but no doubt this was wrong in many cases, for also in Germany the epidemiologic state had altered; here too still more persons left childhood tuberculin-negative. As to the contrast between MALMROS-HEDVALL's and his own investigations FROSTAD is of opinion that the »initial foci» represent a later stage of the pulmonary tuberculosis, viz. the early dissemination from the first established destructive tuberculosis of the lung.

To obtain an explanation of the diverging opinions HEDVALL has undertaken a fresh investigation, partly arranged in the same way as that of FROSTAD (1946). The result, however, is the same as found by MALMROS-HEDVALL 1938, viz. that phthisis usually originates from »initial foci» and not directly from primary foci. HEDVALL tries to explain the disagreement in making the hypothesis, that the origin of phthisis is dependable on the varying gravity with which the tuberculous infection appears in various places. In places where tuberculosis has a severe character phthisis may develop from the primary focus itself, while in places where tuberculosis is more benignant, the first lesions are as a rule characterized by »initial foci». He concludes: »The investigations of FROSTAD and MALMROS-HEDVALL, which include material from places with tuberculosis of varying severity, are not therefore conflicting. On the contrary, they supplement each other in a fortunate way. FROSTAD's cases represent the acute development, those of MALMROS-HEDVALL the subchronic or chronic development after a primary infection.»

In a very interesting treatise (1947) TAGE HYGE accounts for a tuberculosis-epidemic in a school. The source of infection was a lady-teacher with apparently inactive infiltrate-residues with calcifications in both apices. As several circumstances, however, indicated that the infection had been spread by her, she was submitted to tomography, and hereby in her left apex, lateral to a calcification, two small cavities were found. In her gastric lavage + TB. Of 305 pupils:

94 were tuberculin-negative. 70 became invertors. 6 (14.6 %) developed phthisis, 1 died.
106 were B.C.G.-vaccinated. 2 (1.9 %) developed phthisis.
105 were beforehand tuberculin-positive. 4 of these developed phthisis, but only 2 (1.9 %) were certain exogenous, *i. e.* superinfect-infiltrates. (Of the remaining 2, one had to be considered a reactivity-infiltrate, the other as a previously acquired primary infiltrate.)

It appears from this that both the natural acquired allergy and the B.C.G.-vaccination have rendered a remarkable although not an absolute protection against tuberculous infection.

As to the roentgen symptoms found in the 3 groups the following is observed: Amongst the invertors most of them resembled the »subprimary initial foci», only in two cases a destructive process developed directly from primary foci. The two B.C.G.-vaccinated pupils who developed phthisis »showed the altered way of reaction of the allergic organism to the tuberculous infection, the course of the cases being like that observed in patients previously infected with tuberculosis who had gone through a primary infection, for here the initial foci did not appear until nearly one year after the infection and there was no hilar enlargement». — »One Calmette-vaccinated girl who had turned revertor showed similar conditions — which might indicate the presence of some degree of allergy.» In the two previous tuberculin-positive patients who developed phthisis, the first roentgen symptoms, superinfect-infiltrates, in one patient appeared as »dense, spotted infiltration in the right 1st intercostal space»; in the other patient as »small spots behind the right 1st rib and in the right apex», *i. e.* closely corresponding to »subprimary initial foci».

In her Doctors Thesis »On the Fresh Tuberculous Infection» SIGRID HOLM (1947) has in detail accounted for the roentgeneological lesions. The material, originating from the Copenhagen Dispensary, contains 2,298 invertors, of which 1,020 were children. At the first roentgen examination after inversion pathological findings were demonstrated in 437 patients. While the vast majority of patho-roentgenological changes in children was located in the hilar regions, the lesions in the 225 adults were distributed in the following way:

54 had infiltrates similar to the »Frühinfiltrat»,
59 had spotted infiltrations to a limited extend, 46 of these corresponding to »subprimary initial foci»,
18 had voluminous hilar shadows,
18 had extended infiltrations, and
46 had exudative pleurisy.

As the period from the last negative to the first positive tuberculin reaction has varied from 2 months to 2 years, it will in many cases be

impossible to tell anything about the age of the different roentgenologica lesions. It is therefore emphasized that a certain amount of the patho roentgenological changes at the time when the inversion was demonstrated, undoubtedly signify a further development of the primary lesions. Naturally this in particular concerns the forms of infiltrates named as »spotted infiltration to a limited extend» and »more extended infiltration».

Regarding the development to extended phthisis in the cases which in all probability may be signified as primary, »the small demarcated infiltrates», SIGRID HOLM demonstrated 3 ways of development: 1) by cavitation and propagation, 2) by development of new processes in the immediate vicinity of the infiltrate, and 3) by appearance of processes elsewhere in a hitherto unaffected part of the lung. This spread is believed to have emerged bronchogenously, as exhaustively accomplished bacilli researches in all patients successfully resulted in detecting bacilli in the sputum or the gastric lavage in the majority of the cases. Besides, by haematogenous spread one would expect more disseminated lesions.

Finally SIGRID HOLM has examined the pulmonary changes in the invertors where progression does not occur. It is observed that the hilar changes are the first to decline or vanish, while the infiltrates last considerably longer and only a few disappear without leaving a trace. The majority leaves residues behind, often in the form of fibrotic streaks or spots, in many cases with calcifications. In this connection attention is drawn to the very interesting fact that at the first examination calcificated foci were found in 13 invertors indicating previous, now biologically healed tuberculous processes. In other words: *reversion, i. e.* cessation of tuberculous allergy, is not a rare phenomenon, and the *inversion* therefore does not always express a primary infection, but may sometimes — especially in adults — signify a reinfection.

IV. A General View of the Phthisiogenous Forms of Infiltrates

As shown in this brief recapitulation of the most important of the Scandinavian researches during the last few years the »Doctrine of Frühinfiltrat» may now be considered a past phase.

BRAEUNING & REDEKER's demonstration that most phthisis in adults developed from infraclavicular solitary infiltrates was correct to a certain extent, but their interpretation of the genesis had — with the exception of the superinfection — proved untenable. It failed partly due to their inability to disengage themselves from RANKE's Stage-Doctrine, and partly due to their insufficient knowledge of their patients' tuberculin tests.

The recent researches have shown that the »Frühinfiltrat» in most cases is identical with a primary infiltrate, in some cases with a superinfect- or reinfect-infiltrate, and in addition hereto — after the increased

employment of B.C.G.-vaccination — with a post-vaccination-infiltrate. The development to phthisis from these exogenous infiltrates may take place either immediately or after a temporary regression, or phthisis may develop from subsequent secondary endogenous — presumably bronchogenous — foci, corresponding to the »sub-primary initial foci».

Further it is known that a pulmonary tuberculosis may develop from haematogenous foci after secondary spread, possibly also from more isolated haematogenous forms of infiltrates, and finally from reactivated infiltrate-residues in succession to both exogenous and endogenous infiltrates, sometimes after a latent period of several years.

How ever different these forms of infiltrates may be as to genesis, aspect and age, they all have in common that they may form the starting-point for phthisis. They are therefore comprised under the general term: *the phthisiogenous forms of infiltrates.*

To facilitate a general view the preceding forms are arranged as follows:

Phthisiogenous Forms of Infiltrates

I. Exogenous Infiltrates:

1) *Primary infiltrates:* exog. foci in a hitherto non-tuberculous organism.
2) *Superinfect-infiltrates:* exog. foci in a tuberculous-allergic organism.
3) *Reinfect-infiltrates:* exog. foci in a reverted organism.
4) *Post-vaccination-infiltrates:* exog. foci in a B.C.G.-vaccinated organism.

II. Endogenous Infiltrates:

1) *bronchogenous:*
   a) grouped or scattered foci (»Daughter- or Filial-infiltr.» *e. g.* »subprimary initial foci»).
   b) disseminated spread of small foci.
2) *haematogenous:*
   a) disseminated spread, *primarily* as *miliary tuberculosis.* *secondarily* as *»Spätstreuung».*
   b) as isolated *»pluri-focal infiltrates»* corresponding to certain forms of »Frühinfiltrat», described by BRAEUNING & REDEKER (questionable).

III. Residual- or interval-forms:

Infiltrate-residues from exogenous or endogenous infiltrates which in periods of reduced resistance may reactivate moulding the starting-points for phthisis (*»Nachschub»-infiltrates, i. e. »Reatictivity-infiltrates»*).

V. On the Phthisiogenous Infiltrates and the Development of Phthisis

Nowadays in most civilized countries — due to the effective milk-hygiene — the intestinal way of infection must be considered an exception. As a rule it is the air-borne primary focus which carries the tuberculous infection into the organism. *The primary focus* — defined as a caseous pneumonia surrounded by elementary tubercles — in connection with the regional hilar adenitis constitutes the *»primary complex»*. Through a period of 6—8 weeks the primary affection causes an allergy (immunity) of the organism against tuberculosis. Simultaneously with the appearance of the allergy a non-specific perifocal infiltration will often be found round the primary focus. (REDEKER's *»primary infiltration»*, ELIASBERG & NEULAND's *»epituberculous infiltration»*.) It is of importance to know this, because an epituberculous infiltration will often occur at the time when subjective symptoms — initial fever, cough or stitch — may cause a roentgen examination. In some cases, especially in women and children, a simultaneous appearance of *erythema nodosum* is observed, by ERNBERG called »the autogenous tuberculin reaction of the organism».

The primary focus is as a rule solitary, rather homogeneous, more or less clearly demarcated, often circular or oval. The size varies from a bean to that of a prune. It may appear everywhere in the lung, but mostly in the upper part, particularly infraclavicularily. In infants it most often will be found in the hilar region, and as the epituberculous infiltration in children often appears with particular density it is intelligible that it must be in the shape of the so-called *»hilar tuberculosis»*, due to the fact that the perifocal infiltration and the hilar enlargement will fuse, thus giving the well known roentgen picture: voluminous, bushy hilar shadows. On the principle there is no difference between hilar tuberculosis and the ordinary primary complex with focus situated more peripherally.

The fate of the primary focus may now form differently:

1) The caseous content may penetrate to a bronchus and be expectorated *in toto*. The tissue of the small primary cavern is resorbed, and on the roentgen film only a small fibroid scar or a slight vascular density persists. (Residual-form.)

2) The focus may indurate or calcificate. The induration may either be *total* (a-bacillar) or *partial* (bacillar), in the latter case possibility of later reactivity. (Residual-form.)

3) The caseous content may penetrate to a bronchus and give bronchogenous spread, either as disseminated small foci or as a few grouped or scattered larger foci. (»Daughter- or Filial-foci», *e. g.* »sub-primary initia foci».)

4) The primary focus may develop (by propagation) into an acute destructive phthisis, either immediately or after a temporary regression.

The three other forms of exogenous infiltrates all bear the impression of the altered manner of reaction in an allergic organism. None or an insignificant perifocal reaction and no swelling of the hilar glands are observed. This applies also to the reinfect-infiltrate, which one theoretically might expect to act in the same way as a primary focus, but in spite of its occurrence in a reverted organism it acts as if a latent allergy still was present.

The grouped or scattered bronchogenous foci, »the Daughter- or Filial-foci», may originate both from exogenous and endogenous infiltrates. In appearance and size they may resemble the exogenous foci, but contrary to those they are rarely solitary and as a rule they are smaller and less demarcated. Usually they appear in the same lung as the mother-focus, but are sometimes observed in the opposite lung or in both lungs at the same time. Now and then they may be seen as a group of small foci round a bronchial branch (»pluri-focal infiltrate»?). As they develop after the occurrence of the allergy, they usually show less tendency to liquefaction than the primary infiltrates and are not accompanied by perifocal reactions. It is sometimes observed that while the mother-focus itself calcificates or is resorbed, one or some of the filial-foci form the starting-point for phthisis, *e. g.* »the sub-primary initial foci». The bronchogenous foci may, however, also be resorbed or calcificate, or they may persist as apparently inactive infiltrate-residues with possibility of subsequent reactivity.

The bronchogenous disseminated spread is mostly observed at more advanced phthisis, but may occasionally occur early at the acute developed forms of pulmonary tuberculosis.

During the primary infection the bacilli via the lymph vessels have reached the hilar glands, where they cause an *adenitis*, usually of caseous character. This will gradually indurate, often with calcifications. In conformity with the lung-focus this induration may either be total (a-bacillar) or partial (bacillar). By biological cure of both lung- and gland-focus the allergy of the organism will be lost, *i. e.* the organism reverts to its prior stage of tuberculous innocence, at any rate theoretically, for — as mentioned before — some latent allergy seems still to be present. However, the rule is, that once tuberculin-positive, always so, probably because the allergy is preserved by small subsequent superinfections.

If the bacilli survive in the gland-foci the possibility of subsequent haematogenous spread is present at periods when the resistance of the organism for some reason is reduced. This may take place either as *secondary disseminated spread*, *»Spätstreuung»*, or possibly also as more *isolated*

»*pluri-focal infiltrates*», a type of »Frühinfiltrat». The haematogenous genesis of the latter is, however, dubious. Thus LOESCHCKE is of opinion that in all probability the »pluri-focal infiltrate» consists of closely neighbouring, partly confluent bronchogenous foci. Besides, as to the secondary haematogenous spread must be said, that — contrary to prior conception — a stage of generalisation now only exceptionally is considered a link between the primary infection and phthisis. Only where the question is about extra-pulmonary tuberculosis a haematogenous spread must as a rule be assumed. However, it must be emphasized that in the war-damaged Europe of our days the secondary haematogenous spread most certainly is a phthisiogenous form of infiltrate, which must be counted with.

The caseous gland-foci may also penetrate to one of the pleural fissures, which reach closely to the hilus, and produce *effusive pleurisy*, such as demonstrated by the Swedish author O. CARSTENSEN. Through the action of respiration the bacilli are scattered in the pleural spaces, implanting tuberculosis. In such cases a miliary seed of typical tubercles on the pleura may be seen by thoracoscopy. As a rule the primary exudative pleurisy occurs about 6 months after the commencement of the primary affection. It may be considered probable that a pleurisy also may arise by penetration from a sub-pleurally situated lung-focus, but there is scarcely any doubt that the glandular genesis is very frequent.

In some cases the infection is not checked immediately in the hilar glands, but continues via the paratracheal glands and the thoracic duct into the blood. The tuberculous infection enters RANKE's 2nd stage, *the dissemination*. The primary haematogenous spread may develop very differently, dependent on the amount and virulence of the bacilli. *Two types of miliary tuberculosis* are discernible, one *malign* and one *benign*. *The malign miliary tuberculosis* develops as a »Blitz-offensive», immediately paralysing the defence of the organism. *Mantoux* remains negative. None or a slight hilar reaction is observed, and death occurs after the lapse of a few months. Sometimes the progress may be so violent that one must take in consideration the possibility that the passing of the bacilli into the blood has not happened via the glands, but direct from a lung-focus into a small vessel. As to *the benign miliary tuberculosis* there is no doubt that it develops via the glands, as here often considerable swelling of the hilar and paratracheal glands is observed and *Mantoux* turns positive. The *prognosis quo ad vitam* is here good, although the organism at times must fight a severe struggle. Most of the miliary foci will gradually be resorbed, some will calcificate, while others may grow to larger foci and then regress, persisting as infiltrate-residues with possibility of later reactivation. The benign miliary tuberculosis is often accompanied by bilateral effusive pleurisy, here of haematogenous origin.

Finally we have *the infiltrate residues* or the *»Residual- or Interval-forms»*. They may be the remains of both exogenous and endogenous infiltrates and are of a very different appearance. At times they look like *»coarse fibroid residues»*, often with calcifications; in other cases they may appear as slightly striated condensations in one of the intercostal spaces, *»Induration-areas»*, or only as *»local vascular density»* compared with the corresponding area in the opposite lung. BRAEUNING & REDEKER, who have introduced these terms, describe other »Interval-forms» which, however, shall not be mentioned here as to my opinion the differentiation is carried too far. But the authors are no doubt right when they maintain, that great attention must be paid to such residues of infiltrates. They may look very innocent and inactive, but nevertheless they must be looked upon as »the 5th column of the pulmonary tuberculosis». Some of them may contain bacilli-foci and may in periods of reduced resistance of the organism — due to infectious diseases, undernourishment, fatigue, etc. — suddenly wake up and be active again, forming what BRAEUNING & REDEKER name as »Nachschub»-infiltrates (reactivity-infiltrates), which at times may develop to destructive phthisis.

VI. Some Examples of Phthisiogenous Infiltrates

The Central Tuberculosis Dispensary in Copenhagen possesses a great material covering all forms of phthisiogenous infiltrates. In a periodical publication as the present it will only be possible to show a small selection. I have endeavoured to find a few typical representatives from all 3 groups. Cases of dissemination and hilar tuberculosis are excluded as they must be considered well known. To attain the clearest possible appearance of the small lesions so characteristic of many of the phthisiogenous forms of infiltrates, as a rule photos in detail and in natural size are shown. The disease-records are confined to the necessary minimum.

Case 1. Example of »primary infiltration» or »epituberculous infiltration».

♂ 19 years. Invertor. Cough a few months. Feeling well.

Fig. 1. (6. 1. 36) Rather dense, cloudy infiltration in the right clavicular-mediastinal triangle. Voluminous right hilar shadow. Left lung normal. Gastric lavage: + TB. — *Fig. 2.* (20. 8. 36) 7 months later after treatment at sanatorium. The perifocal infiltration has now disappeared and the primary focus is seen in the right 1st intercostal space. Gastric lavage: ÷ TB. Later complete resorption of focus.

Case 2. Example of primary infiltrate which after temporary regression reactivates and forms a starting-point for greater infiltration.

♀ 11 years. School-invertor. Feeling well.

Fig. 3. (29. 10. 40) Small primary infiltrate in the left 3rd intercostal space. — *Fig. 4.* (25. 11. 41) About a year later. Regression. Now only slight vascular density

Fig. 1.

Fig. 2.

in the 3rd intercostal space. (*Residual-form.*) — *Fig. 5.* (14. 3. 44) $2^1/_2$ years later. Now reactivity of the infiltrate-residue with spotted infiltration in the left 2nd and 3rd intercostal space. Gastric lavage: + TB. Later again regression after treatment.

Case 3. Example of destructive phthisis derived from a primary infiltrate with bronchogenous spread to the upper part of the opposite lung.

♀ 3 years. School-invertor. Feeling well.

Fig 6. (9. 2. 40) Primary infiltrate in the left 6th intercostal space. Gastric lavage: + TB. The mother does not want her child admitted to sanatorium, but keeps her at home. — *Fig. 7.* (8. 4. 42) 2 years later. Now considerable infiltration with cavity in the left base and bronchogenous spread in the upper part of the right lung. — Later florid phthisis.

Case 4. Example of a superinfect-infiltrate which after a stationary period suddenly expands and undergoes cavitation. Regression after treatment.

♀ 22 years. In June 1937 tuberculin-positive with normal radiogram.

Fig. 8. (26. 10. 38) Has for some time lived with a sister suffering from phthisis. In the right 1st intercostal space is seen a small round infiltrate. Only moderate hilar reaction. Gastric lavage: + TB. — *Fig. 9.* (25. 2. 41) Control examinations during 1939—40 had shown the infiltrate unchanged, but it has now grown and a large cavity is observed. Sputum: + TB. — Admitted to hospital, later transferred to sanatorium. Good effect after pneumothorax treatment. At roentgen examination in 1947 no trace of the infiltrate.

Case 5. Example of a superinfect-infiltrate from which a bilateral cavernous phthisis develops.

♂ 24 years. At previous examinations tuberculin-positive with normal roentgen

picture. For some months engaged to a girl who proves to have a desolate cavernous phthisis. She dies 6 months later. He is examined owing to his fiancé's illness. Feeling well.

Fig. 10. (10. 6. 41) A small infiltrate in the left 2nd intercostal space. Gastric lavage: + TB. — Control-examinations during the following months show growth of the infiltrate, but in spite of repeated earnest appeals the patient refuses to be transferred to hospital, as he wants to pass an examination. *Fig. 11.* (10. 7. 42) 13 months later. He has now passed his examination and is willing to be treated, but now he has a bilateral cavernous process. — Since then suffering from phthisis.

Fig. 3.

Case 6. Example of »sub-primary initial foci» as starting-points for phthisis.

♂ 32 years. In June 1940 tuberculin-negative with normal radiogram.

Fig. 12. (13. 1. 41) Now Mantoux +. Small-spotted infiltration in the right apex and larger, round focus in the right 1st intercostal space. A small spot in the left apex. (Possibly the focus in the right 1st intercostal space represents the primary infiltrate.) Gastric lavage: ÷ TB. — Repeated roentgen examinations during 1941—42 show unchanged conditions, but in April 1942 is demonstrated + TB in the gastric lavage, and he is transferred to a sanatorium for some months. After a period of vagrancy he is again exam-

Fig. 4.

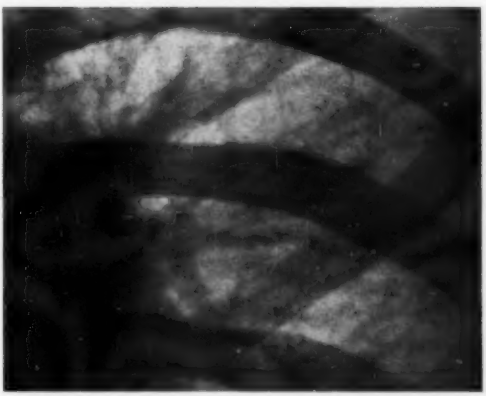


Fig. 5.

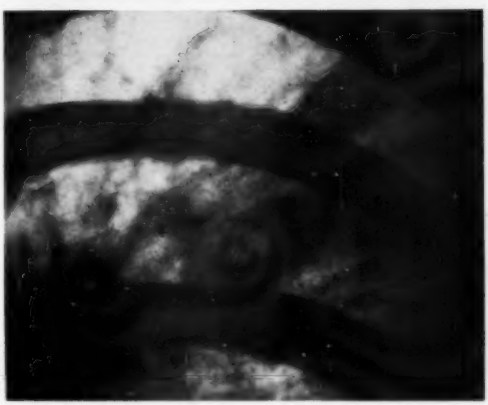


Fig. 6.

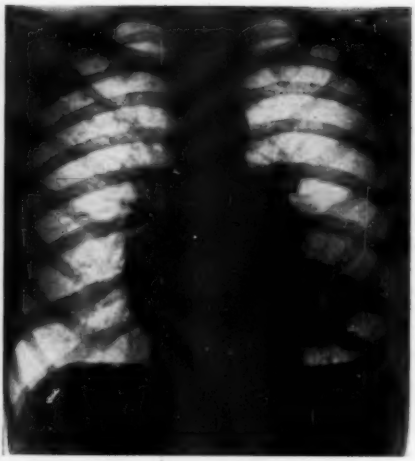


Fig. 7.

Fig. 8.

Fig. 9.

ined 13. 11. 44. *Fig. 13.* Now dense infiltration in the right apex and the 1st intercostal space with a large cavity. Sputum: + TB. He is transferred to hospital, where he dies 5 months later.

Case 7. Example of 2 closely neighbouring endogenous, possibly haematogenous, infiltrates from where a destructive phthisis develops.

♀ 25 years. From a tuberculous home. As child she herself had pulmonary tuberculosis. Since then tuberculin-positive. Feeling well.

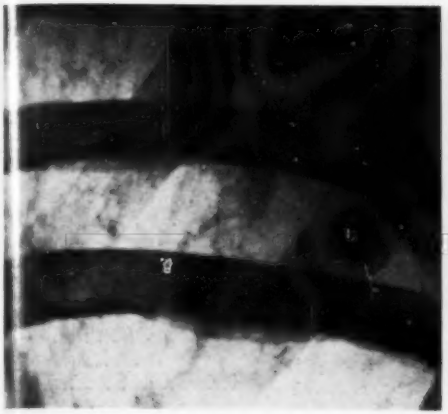


Fig. 10.

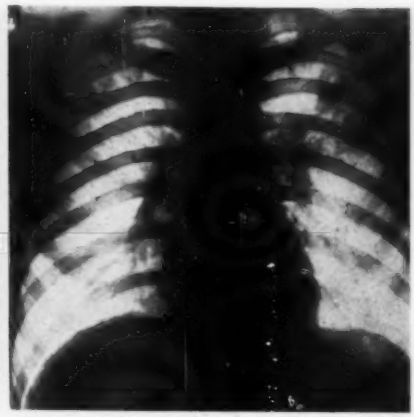


Fig. 11.

Fig. 12.

Fig. 13.

Fig. 14. (27. 1. 36) In the left 1st intercostal space 2 small infiltrates. Control-examinations during 1936—37 show unchanged conditions. *Fig. 15.* (26. 11. 37) Cough one month. Now a large infiltration with cavity in the left infraclavicular region. Sputum: + TB. Admitted to hospital, where thoracoplasty is applied, but the process develops and she dies 6 months later.

Case 8. Example of an endogenous »pluri-focal« infiltration as starting-point for bilateral cavernous phthisis.

♀ 15 years. From a tuberculous home. Tuberculin-positive for several years. Previous radiograms negative. Feeling well.

Fig. 16. (5. 4. 37) A pluri-focal infiltration behind the sternal end of the right second rib, and a small soft spot in the right 2nd intercostal space. Enlarged right para-

Fig. 14.

Fig. 15.

Fig. 16.

Fig. 17.

tracheal gland, possibly sign of a preceding generalisation. *Fig. 17.* (30. 8. 37) About 3 months later. Now extended infiltration with cavity in the upper part of the right lung Sputum: + TB. Later bilateral phthisis.

Fig. 18.

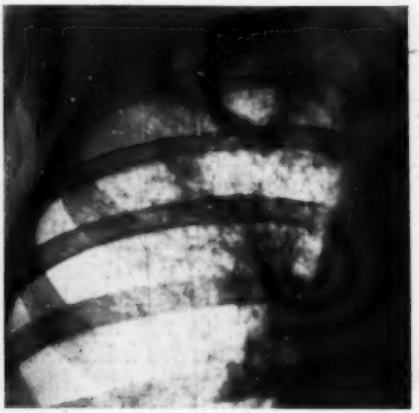


Fig. 19.

Case 9. Example of reactivity of an infiltrate-residue, »Residual-form» (*»coarse fibroid residues with calcifications»*).

♀ 27 years. Pleurisy 5 years old, treated at home. Thence no roentgenogram, but it is probable that there has been at the time a tuberculous infiltration in the upper part of the right lung. At an examination 1944 she was tuberculin-positive, and the radiogram showed fibroid spots with calcifications in the right apex and the 1st intercostal space. Gastric lavage: ∴ TB.

Fig. 18. (23. 4. 47) Feeling well. The roentgenogram identical with that in 1944. Gastric lavage: ∴ TB. — In the autumn 1947 she is treated for *abscessus ad anum*, is feeling fatigue and looses in weight. *Fig. 19.* (17. 11. 47) Now a large infiltration in the right apex and infraclavicular region with a cavity in the 1st intercostal space. Sputum: + TB. Admittance to hospital.

VII. Conclusion

The purpose of this article has been to emphasize that a destructive phthisis may develop from infiltrates or residues of infiltrates, different as to genesis, aspect and age. They are comprised under the general term: phthisiogenous forms of infiltrates.

How the development of phthisis proportionally is divided among the various forms of infiltrates is difficult to tell, as it often is impossible to decide what kind of infiltrate one encounters on the roentgenogram in the specific case. This applies especially to the exogenous forms of infiltrates. To express any opinion of the genesis with just a fair certainty, complete anamnestic and clinical informations are necessary, and such are not always available. Thus one must be precisely aquainted with

previous and present tuberculin reactions of the patient, and preferably also be able to compare with previous roentgen photos.

However, later years' researches apparently show: 1) that most phthisis probably develops either direct from primary infiltrates or from early originated bronchogenous filial-infiltrates, 2) that exogenous foci in an allergic or reverted organism are less disposed to be »phthisiogenous», but in some cases *may* be so, 3) that a phthisis *may* develop from persistent foci subsequent to haematogenous spread, and 4) that apparently inactive infiltrate-residues in periods of reduced resistance at times *may* reactivate and develop to destructive phthisis.

For the practical work at dispensaries and at mass investigations it is of subordinate value whether the examiner can differentiate the various forms of phthisiogenous infiltrates, but it is of great importance that he knows them. For some of these often barely discernible and at times innocently looking lesions may — sooner or later — mould starting-points for phthisis. They must therefore not be overlooked, and they ought to be controlled at not too long intervals.

SUMMARY

Based on later years' literature and experiences from the Central Tuberculosis Dispensary in Copenhagen it is demonstrated that a destructive phthisis may develop from infiltrates or residues of infiltrate of different genesis: 1) *Exogenous foci:* Primary-, Superinfect-, Reinfect- and Post-vaccination-infiltrates. — 2) *Endogenous foci:* bronchogenous or haematogenous, and 3) *Residual- or Interval-forms:* infiltrate-residues after either exogenous or endogenous infiltrates. — These different forms of infiltrates are comprised in the general term: *phthisiogenous forms of infiltrates.*

ZUSAMMENFASSUNG

Auf Grundlage der Literatur der letzteren Jahre und der Erfahrungen der Zentral-Tuberkulosefürsorgestelle in Kopenhagen wird nachgewiesen, dass eine destruktive Phthisis sich aus Infiltraten oder Infiltrat-Residuen verschiedener Genese entwickeln kann: 1) *Exogene Foci:* Primär-, Superinfekt-, Reinfekt- und Post-Vaccinations-Infiltrate. 2) *Endogene Foci:* bronchogene oder haematogene, und 3) *Residual- oder Intervalformen:* Infiltrat-Residuen nach entweder exogenen oder endogenen Infiltraten. — Diese verschiedenen Infiltratformen werden unter der gemeinschaftlichen Benennung: *phthisiogene Infiltratformen* zusammengefasst.

RÉSUMÉ

Sur la base de la littérature de ces dernières années et des expériences de la Dispensaire de tuberculose de Copenhague on démontre qu'une phthisie destructive peut se développer d'infiltrates ou des infiltrates-residus d'une genèse différente: 1) des *foci exogènes:* des infiltrates primaires, superinfectes, réinfectes et post-Calmettes. 2) des *foci endogènes:* bronchogènes ou haematogènes, et 3) des *formes résiduales ou intervalles:* des infiltrates-résidus d'après des infiltrates exogènes ou endogènes. — Ces différentes formes d'infiltrates se résument sous la designation commune: des *formes d'infiltrats phthisiogènes.*

REFERENCES

ASSMANN, H.: Klinische Roentgendiagnostik innerer Erkrankungen. (2. Aufl.) Leipzig 1922.

BRAEUNING, H. & F. REDEKER: Die hämatogene Lungentuberkulose des Erwachsenen. Tuberk. Bibl. 38.

BRAEUNING, H. & F. REDEKER: Phthisische Entwicklungen aus den Reihen des Frühinfiltrates und des frühen phthisischen Nachschubes. Tuberk. Bibl. 39.

CARSTENSEN, O.: Om Tuberculosis pleurae exsudativa. — Nord. Med., Nr. 43 — 1940.

FROSTAD, S.: Tuberculosis incipiens. Acta tub. scand. Suppl. XIII. 1944.

HEDVALL, E.: Tuberculosis incipiens. Stockholm 1946.

HEIMBECK, J.: Infektion und Erkrankung bei Tuberkulose. Acta med. scand. Suppl. LIX. 1934.

HOLM, SIGRID: Om den friske tuberkulose Infektion, dens Klinik, Prognose og Behandling. (Doctoral Thesis) Copenhagen 1947.

HYGE, T. V.: Epidemic of Tuberculosis in a State Scool. Acta tub. scand. XXI, 1947.

LOESCHCKE, H.: Über Entwicklung, Vernarbung und Reaktivierung der Lungentuberkulose Erwachsener. — Beitr. klin. Tbk. 68. 1928.

MADSEN, TH., J. HOLM & K. A. JENSEN: Studies on the Epidemiology of Tuberculosis in Denmark. — Acta tub. scand. Suppl. VI. 1942.

MALMROS, H & E. HEDVALL: Studien über die Entstehung und Entwicklung der Lungentuberkulose. — Tub. Bibl. 68. 1938.

SCHEEL, O.: Primo-Infection tuberculeuse de l'adolescent et de l'adult. Rapport X, Conferencia União Intern. Tuberculose. — Lisboa 1936.

FROM THE ROENTGEN DEPARTMENT OF THE SERAPHIMER HOSPITAL, STOCKHOLM
(ACTING CHIEF: E. LINDGREN)

ELECTROKYMOGRAPHY WITH SIMULTANEOUS ELECTROCARDIOGRAPHY[1]

by

Ture Andersson

Electrokymography with Simultaneous Electrocardiography

During the past decade, research has been carried on in the Roentgen department of the Seraphimer Hospital with a view to producing a better method of kymography than the ordinary method with a screen kymograph. During the years 1937—1939, endeavours were made to record the variations of fluorescent light during the irradiation of the heart with the help of photo-electric cells and amplifiers. The photocells available, however, did not furnish any satisfactory results. Efforts were therefore made to discover more suitable indicators and, in 1946, HJELMARE showed that variations in intensity, caused by movements of the heart, could be recorded by means of Geiger-Müller counters of special construction, provided with suitable amplifying devices. As early as 1945, however, BOONE and HENNY described an apparatus, based on the principle of the photocell, with which they could make satisfactory recordings of the movements of the heart. As indicator they used a photomultiplier tube and called their method electrokymography.

At the Seraphimer Hospital, we have used this method since the summer of 1947. The photomultiplier tube is, in principle, a photoelectric cell with considerable self-amplification. It is most sensitive to visible light, but is also influenced to a lesser degree by roentgen rays.

The photomultiplier tube is enclosed in a double casing, the outermost consisting of a lead case provided with a longitudinal slit measuring $^1/_2 \times 4$ cm. Inside the lead case there is a casing of black paper for the exclusion of visible light. Next to the photo tube is a fluorescent layer which is free from inertia. The photomultiplier tube is attached to a 220 volt A. C. supply through a voltage divider connected to a high tension 1000—1200 volt rectifier. The electric currents produced in the photomultiplier

[1] Submitted för publication, May 8, 1948.

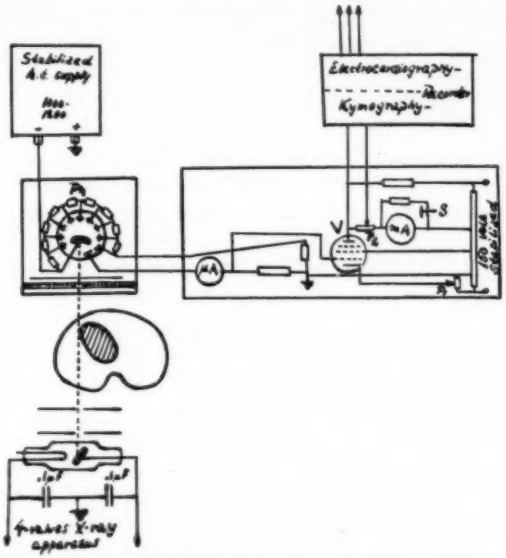


Fig. 1. Diagram of the essential parts of the apparatus. The radiation from the roentgen tube which is supplied with direct tension strikes the cathode of the photomultiplier tube (Ph) after having passed along a passage, provided with a light-proof shield, in the lead casing which surrounds the tube. The current from Ph is indicated by the microammeter (μA), amplified in (V) and conducted to the kymograph portion of the electrocardiograph. The amplitude of the kymogram can be varied by means of (P_2). The plate current of the amplifier valve is counterbalanced in the oscillograph portion and the milliammeter (mA), and the correct working point is obtained by varying the grid-bias by means of (P_1) in such a way that (mA) is adjusted to zero. By means of the switch (S), (mA) is shunted to a less sensitive scale at the commencement of the adjustment process.

tube by the influence of light are conducted through an amplifying and stabilising device to a recording galvanometer. We have made use of one of the galvanometers in an electrocardiograph (Elmqvist system) in which two of the galvanometers can be disconnected from the electrocardiograph amplifiers. By this arrangement, the variations of current are shown as a continuous curve and, at the same time, we have been able to make an electrocardiogram (fig. 1).

Up to the present, we have carried out examinations with patients in the recumbent position. During the examination the patient is irradiated with the centre beam adjusted at a tangent to the point of the heart's contour of which it is desired to record the movements, using a primary stop which gives a field of about 5 cm. diameter on the irradiation screen. The photomultiplier tube is placed against the patient's thorax with the

slit at right angles to the point on the contour of the heart in question in such a manner that the centre beam passes through approximately the centre of the slit. Under the influence of the roentgen rays the fluorescent layer affects the photomultiplier tube with light of varying intensity in accordance with the movements of the contour of the heart which cause a varying degree of absorption of the roentgen rays under the slit. The patient should hold his breath during the recording of the curve.

In our examinations we have used a current of from 2—3 mA and a tension of from 50—70 kV with a focus distance to the skin of about 60 cm. 1 mm. Al filter was used.

We have been able to record the movements of the heart in most cases, even where the patient was very massive and the pulsations of the heart showed themselves to be small during irradiation. In patients with stasis of the lungs, the heart movements were, however, only recorded with difficulty in many cases and in two cases it was quite impossible to obtain any results.

In this connection, it should be observed that the amplitude of the movements of the heart is not recorded by this method. The swing of the galvanometer is adjusted according to a number of variable factors, such as the intensity of the roentgen rays, the voltage on the phototube and the setting of the potentiometer which must necessarily be varied according to the patient's permeability to roentgen rays.

The Americans BOONE, HENNY, CHAMBERLAIN and several others have, in the course of their researches, taken a carotid sphygmogram simultaneously with the electrokymogram which they interpreted by comparing corresponding time points on both curves. The advantage of this method is that the carotid pressure curve has several well-marked points with a fixed relation to certain phases of the heart cycle. The above mentioned authors have also experimented with simultaneous phonocardiograms and electrocardiograms, but they consider that the carotid sphygmogram is superior as a comparative curve. Against the electrocardiogram they observe that it shows much too great variations in time in relation to the electrokymogram.

In all cases we have made simultaneous electrocardiogram recordings and we have endeavoured to interpret the electrokymogram partly by comparison with the curves obtained from the different chambers of the heart and the great arteries and partly by comparison between the electrokymogram and the electrocardiogram.

We have connected up the galvanometer in such a way that the rise of the curve represents diminished intensity, which, to a great extent, marks the dilatation of the heart, while the fall of the curve represents increased intensity, corresponding to the contraction of the heart. It should, however, be observed that in addition to the change in volume

the heart performs an oscillatory and rotary movement which to a certain extent influences the curve. Increased or diminished intensity can also be brought about by a change in the shape of the heart without a change in the volume. This occurs in the isometric contraction and relaxation phases.

We have examined about 125 patients who showed no clinical or roentgenological signs of disease of the heart. These comprise nearly twice as many men as women. Their ages varied from 17 to 66 years. In addition, we have examined a smaller number of patients with cardiac trouble. The following descriptions are based almost entirely on normal cases.

The Ventricles

The left ventricle has been examined by means of recordings made over the left contour of the heart with the patient in a recumbent position and over the posterior, lower contour of the heart in a lateral posi-

Fig. 2. Curve from the left ventricle.

tion. The movements of the right ventricle have been examined by means of recordings over the anterior contour of the heart in a lateral position or with the patient turned towards the right. The curves obtained in this manner have a uniform shape and a typical position in relation to the electrocardiogram (fig. 2). They consist of a long rising portion and of a shorter falling one. The former, which in the main represents the diastole of the ventricle, begins a short time after the T wave and at first rises relatively steeply, developing a more horizontal course in its later stages. Between the R and T waves it changes over to the other, fairly steep, falling systolic portion.

In the even course of the curve, a number of breaks occur in characteristic positions. These we endeavoured to interpret by comparison with the corresponding auricular and arterial curves on the basis of known conditions of the physiology of the heart. The more horizontal course of the curve during the latter part of the diastole of the ventricle is broken after the P wave by a more or less sharply marked passage to a steeper

rise due to the accelerated dilatation of the ventricles caused by the auricular systole. In the transition period between the diastole and the systole the curve shows a short horizontal stretch or in many cases a dip. On the basis of the carotid sphygmogram, the American writers have shown that this portion of the ventricle curve coincides with the isometric contraction. By comparison with the electrocardiogram, the isometric contraction takes place between the R and T waves and agrees in position with that portion of the aorta or pulmonary artery curve which corresponds to the isometric contraction phase. The curves obtained over the aortic arch and pulmonary artery have in fact an appearance corresponding to that of the sphygmogram of the arteries. During the transition from systole to diastole there is a peak of varying distinctness consisting of a short rising branch and a short falling one. This peak is in the same position in relation to the electrocardiogram as the dip in the artery curve which corresponds to the closing of the aortic and pulmonary valves. If the top of the peak corresponds to the closing of the aortic and pulmonary valves, its first branch should in the main correspond to the protodiastole and its second branch to the isometric relaxation.

In this way, during the isometric contraction and relaxation phases, small changes in the direction of the curve occur although the heart does not alter in volume. The American writers explain these as »positional changes», that is to say changes of form without change of volume or rotation of the heart. STUMPF has represented the corresponding peak on a densogram curve during the isometric contraction phase as depending on a physiological regurgitation through the orifices together with the closing of the aortic valves. Thus, according to STUMPF, a physiological aortic insufficiency should exist. The described changes in the ventricle curve in connection with the opening and closing of the valves are in many cases only slightly marked and may be entirely absent (fig. 3).

Frequently, in comparing the arterial and the ventricular curves, it may be found that the closing of the aortic valves corresponds to a point a little way op on the curve's rising portion and that it is often marked there by a peak. This must also be explained by the earlier quoted change of form of the heart during the isometric relaxation phase and rotation of the heart or by a physiological aortic or pulmonary insufficiency.

In comparisons between the curves from both ventricles, no characteristic disparities have been observed (fig. 4).

In a number of cases we have measured the smallest angle through which a patient had to be turned to the right before it was possible to obtain the ventricle curve over the right contour of the heart so that we might obtain a relative measurement of the extension of the right ventricle towards the right. This has shown that the variations are very great. In one case we obtained the ventricle curve with the patient lying flat on his

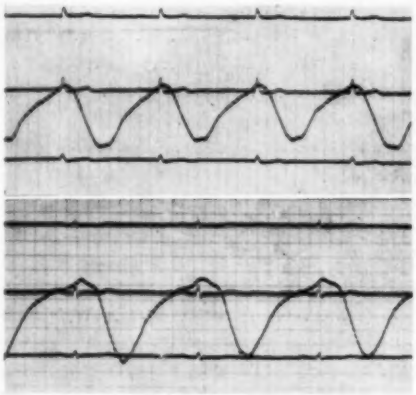


Fig. 3. Two examples of curves from the left ventricle in which the isometric contraction and relaxation phases are only marked faintly or not at all.

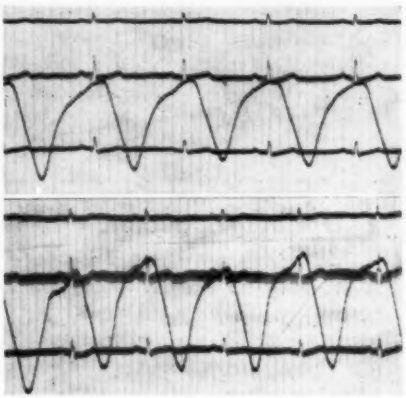


Fig. 4. Curves from both ventricles in the same patient. Above — the left, below — the right ventricle.

back, while in other cases it was necessary to turn the patient through 30—40° to the right before the ventricle curve over the right contour could be obtained.

The Auricles

The movements of the auricles have been examined by recordings made over the right contour of the heart and the left auricular appendage with the patient on his back and over the upper parts of the posterior contour with the patient in the lateral position.

The curves obtained in this way present a markedly different appearance in contrast to the ventricle curves. The movements of the heart's contour are determined by several factors but the diastolic dilatation and systolic contraction of the ventricles dominate the movements in those parts of which the ventricles form the edges. Where the auricles form the edges the movements of the contour of the heart may, however, be determined to as great an extent by the movements of the ventricles as of the auricles. It appears that this influence of the ventricles varies greatly from case to case and it is unequally marked in different parts of the auricles. Thus it is greater the nearer to the annulus fibrosus and the ventricle the edge-forming part of the auricles lie. Furthermore, the influence of the ventricles is less in the upper parts of the auricles.

The curves which we consider most clearly reproduce the movements of the auricle have been obtained over the upper and medial parts of the

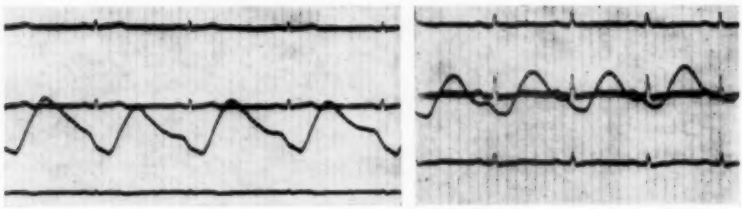


Fig. 5. Curves from the right and left auricles.

right contour of the heart and over the upper part of the posterior contour (fig. 5). From a point between the R wave and the T wave these curves take a relatively sharply rising course depending on the fact that the auricles, after the closing of the atrioventricular valves, are filled with blood from the venae cavae and are dilated. The maximum rise corresponds in time with the isometric relaxation phase in comparison with the corresponding ventricle curve. Thereafter, the curve shows at first a

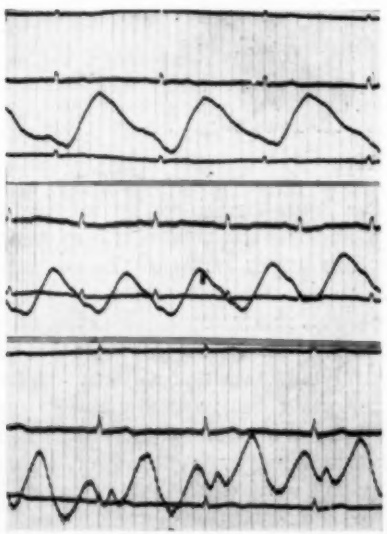


Fig. 6. Right auricle. a) With the patient in a recumbent position. b) With the patient rotated to the left. In both cases »pure» auricle curves. c) With the patient rotated to the right, influence of the ventricle is present.

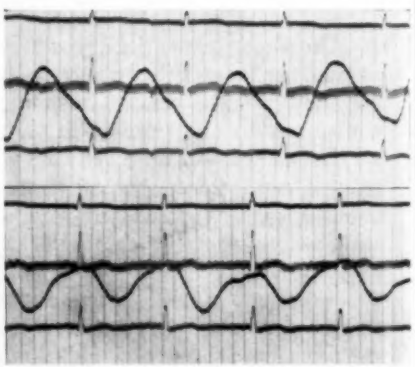


Fig. 7. Right contour. »Pure» auricle curve with the patient in the recumbent position (above). With the patient moderately rotated to the right, a ventricle curve is obtained (below).

fairly steep and later a more gradual fall. This signifies that on the opening of the atrioventricular valves, when the ventricular pressure during the isometric relaxation is lower than that of the auricle, a part of the blood in the auricles flows fairly quickly into the ventricles, whereby the volume of the auricles is diminished. After this initial pouring out the volume of the auricle only undergoes restricted changes until the auricle systole supervenes during the last part of the ventricle diastole which is represented by a sharper fall in the last part of the curve.

Support for our contention that this curve most nearly represents the true movements of the auricle has been obtained from recordings over the right contour with the patient at different angles (figs. 6 & 7). If the patient is turned to the left, *i. e.* when the right ventricle is far removed from the right contour, the influence of the ventricle is diminished and the described curve is obtained in its purest form. In many cases the

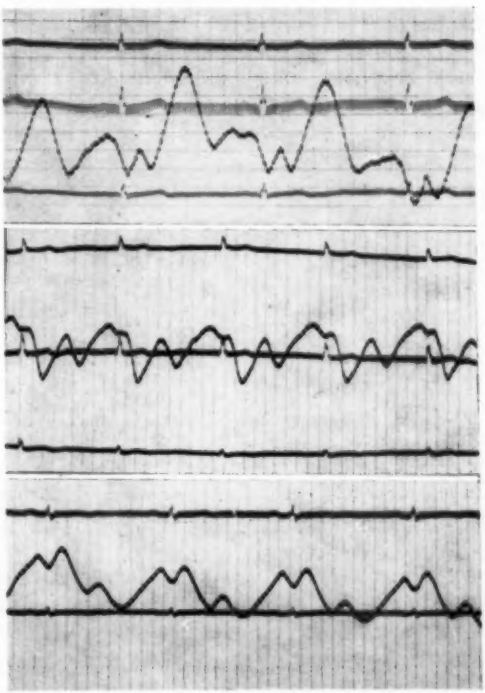


Fig. 8. Curves over the auricle contour showing different degrees of influence of the ventricle.

auricle systole is also found to be more clearly marked on the curve. If. on the other hand, the right ventricle is moved nearer to the right contour by turning the patient to the right, the influence of the ventricle is increased.

If the influence of the ventricle is comparatively great, the curve presents a fairly characteristic appearance with three well defined peaks (fig. 8). The first of these, with its maximum corresponding to the isometric relaxation of the ventricle, corresponds to the filling of the auricle before and the emptying of it after the opening of the atrioventricular valves. The fall in the curve, which represents the emptying of the auricle, changes at a certain point, varying in time according to the amount of the influence of the ventricle, to a rise depending on the fact that the diastolic dilatation of the ventricle causes the auricle contour to displace itself outwards. In connection with the P wave this rise changes into a fall during the systolic contraction of the auricles. The last part of the curve again shows at first a rise and later a fall which is dependent on the last part of the ventricle diastole and on its systole, as well as, to a certain degree, on the change of form of the heart during isometric contraction. To sum up, it may be stated that the maxima of the curve, have, in the main, fixed positions corresponding to the opening of the atrioventricular valves, the commencement of the auricular systole and the commencement of the ventricular systole, while the position of the minima varies according to the amount of the ventricle's influence.

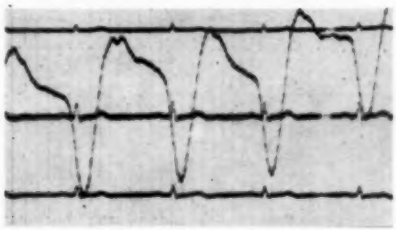


Fig. 9. Curve over the left contour at the left auricular appendage. Influence from the pulmonary artery.

Curves of this type are generally obtained over the lower parts of the right contour and over the left auricular appendage, *i. e.* over parts of the auricles which are more intimately related to the ventricles. The described points are marked to a very varying degree according to the amount of the influence of the ventricle.

On auricle curves, recorded over the upper parts of the right contour and the left auricular appendage, there is also occasionally to be found

the influence of the great branches of the pulmonary artery. The maximum of the curve may then be situated earlier than in the pure auricular curve (fig. 9).

The Arteries

The curves recorded over the aorta and the pulmonary artery present mainly the same appearance as an arterial sphygmogram (figs. 10 & 11). They consist therefore of a sharply rising part which commences in conjunction with the corresponding expulsion phase of the ventricle. After the sharp rise during systole, the curve passes on to a slowly falling portion, in the first part of which a dip is found corresponding to the closing of the aortic and pulmonary valves. Just as in the sphygmogram, the isometric contraction of the ventricles may be indicated on the curve and a small wave is also often to be found, corresponding to the auricular systole. Arterial curves of this appearance have been obtained over the aortic knob and over the pulmonary artery and its branches. The different phases are generally better marked on the aorta curve than on the pulmonary artery curve. These curves seem to be conditioned essentially by the wave of pressure.

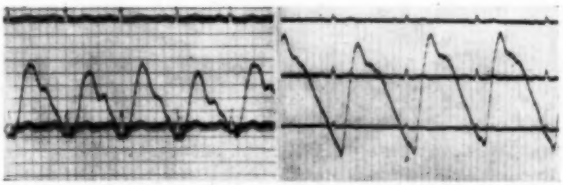


Fig. 10. Curves over the aortic knob.

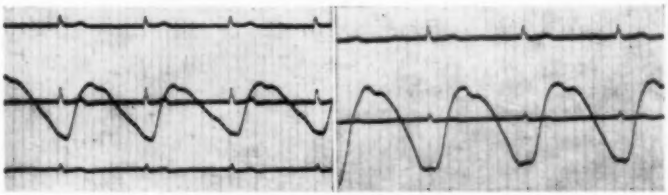


Fig. 11. Curves over the pulmonary artery.

On the other hand, in most cases, the curves over the ascending and descending aorta present a quite different appearance, which would seem to depend on the fact that in this case the oscillatory movement of the

aorta is recorded to a greater degree than over the arcus. In the curves obtained over the ascending aorta the influence of the left ventricle is often clearly present: this was especially marked in the cases of hypertension we examined (fig. 12). It is also probable that the vena cava superior can influence curves recorded over the ascending aorta.

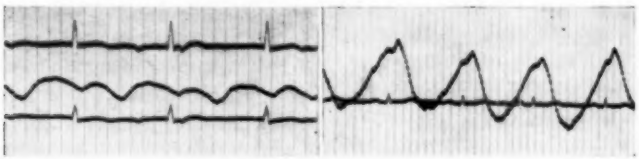


Fig. 12. Curve over the ascending aorta in a normal case (left) and in a case of hypertension (right).

Time relation

With the electrokymogram, BOONE, HENNY, CHAMBERLAIN and their collaborators have taken simultaneous carotid sphygmograms of which the lag, consisting partly of the time needed for the pulse-wave to reach the part of the artery under examination and partly of the conduction factor of the mechanical recording system, can be satisfactorily calculated. The sphygmogram presents certain advantages as a comparative curve because it possesses some easily recognised, physiologically determined points. Since both curves have a common time axis, corresponding points on the electrokymogram can be read off directly.

There is not, however, the same fixed relation between the electrocardiogram and the movements of the heart, and, for this reason, only the principle features of the electrokymogram can be determined by direct comparison between the two curves. Our method of procedure in examination of details has therefore been to compare the curves obtained from different parts of the heart. The kymogram from the great arteries presents, as described before, in the main, the same appearance as the arterial sphygmogram and has therefore served as a basis for the interpretation of the curves from other parts of the heart. By means of the simultaneously recorded electrocardiogram, it has been possible to determine the time relations, whence we have as a rule calculated the distance from the R wave to the different points on the elctrokymogram.

The simultaneously recorded electrocardiograms and electrokymograms always have a typical and mainly constant reciprocal position, but certain time variations are met with, determined to a great extent by the frequency of the heart. In order to make the time relations clear, the

values for some points on the electrokymogram, calculated in seconds from the R wave, have been tabulated below.

Opening of the aortic valves	0,07—0,14	sec. after the R wave
Closing of the aortic valves	0,38—0,49	» » » » »
Opening of the atrioventricular valves	0,41—0,54	» » » » »
Commencement of the auricular systole	0,07—0,11	» before » » »

Heart cycle ..... about 0,70—1,20 seconds, corresponding to a heart frequency of about 50—85/min.

To a great degree it is true that the distance from the R wave to a certain point on the electrokymogram is longer with a slow than with a quick rhythm. This distance is, however, not directly proportional to the length of the heart cycle.

The apparatus for tension stabilization and amplification was designed and constructed by GEORG FREDZELL, civil engineer.

SUMMARY

The author gives an account of the methods of electrokymography as practised in the roentgen department of the Seraphimer Hospital. A short description of the apparatus is given. A photomultiplier tube is used as indicator. The procedure for interpreting electrokymograms is set out. The time relations are determined by means of the simultaneously recorded electrocardiogram. A description of normal electrokymograms from the ventricles, the auricles and the great arteries is given.

ZUSAMMENFASSUNG

Verf. berichtet über die in der Röntgenabteilung des Serafimerkrankenhauses verwendete Elektrokymographiemethode. Es wird eine kurze Beschreibung der Apparatur gegeben. Ein Photomultiplikator wird als Indikator verwendet. Das Verfahren beim Deuten der Elektrokymogramme wird gebracht. Die zeitlichen Relationen werden mit Hilfe des synchron aufgenommenen Elektrokardiogramms bestimmt. Die normalen Elektrokymogramme der Kammern, der Vorhöfe und der grossen Arterien werden beschrieben.

RÉSUMÉ

L'auteur expose les méthodes d'électrokymographie telles qu'elles sont utilisées dans le Service radiologique de l'Hôpital des Séraphins. Il décrit brièvement l'appareil. Un photomultiplicateur sert d'indicateur.

La manière d'interpréter les électrokymogrammes est précisée. Les relations dans le temps sont déterminées par la prise simultanée d'un électrocardiogramme.

Suit la description d'électrokymogrammes normaux des ventricules, des oreillettes et des grandes artères.

REFERENCES

1. Boone, B. R., Chamberlain, W. E., Gillick, F. G,, Henny, G. C. and Oppenheimer, M. J.: Am. Heart J. 1947. 34. 560.
2. Chamberlain, W. E.: Acta Radiol. 1947. 28. 847.
3. Henny, G. C. and Boone, B. R.: Am. J. Roentgenol. 1945. 54. 217.
4. Henny, G. C. and Boone, B. R.: Am. J. Roentgenol. 1947. 57. 409.
5. Hjelmare, G.: Acta Radiol. 1946. 27. 334.
6. Stumph, P., Weber, H. H., Weltz, G. A.: Röntgenkymographische Bewegungslehre innerer Organe. 1936.

FROM THE CLINICAL DEPARTMENT AND THE RESEARCH LABORATORIES, RADIUM CENTRE FOR JUTLAND (CHIEF: PROF. DR. C. KREBS), UNIVERSITY OF AARHUS, DENMARK

CHEMOTHERAPY IN LEUKEMIA, HODGKIN'S DISEASE, AND ALLIED DISORDERS[1]

by

Jørgen Bichel, M. D.

Introduction

A survey of chemotherapeutic agents in leukemia will to a certain extent be a survey of the chemotherapy in cancer, for whenever a new substance capable of inhibiting the growth of cancerous tumours has been found, it almost invariably appears that the effect of the substance will manifest itself much more potently on the hyperplastic disorders of the blood-forming organs, *i. e.*, especially the leukemias. I do not intend to deal with the various forms of hormone treatment of cancer, which cannot be termed chemotherapy in the proper sense of the word, nor do I intend to discuss the form of therapy consisting of direct application of chemicals to or in tumours, where there is often a direct, local caustic effect.

It may be asked whether with our present knowledge there will be any probability of finding a general chemotherapeutic agent in the treatment of cancer in analogy with agents capable of fighting infections caused by known micro-organisms.

Chemotherapy in infections is based on the fact that bacteria are different from the normal cells of the organism, both genetically and with regard to vital metabolic processes. The latter difference explains why it is possible to interfere with the vital processes of the micro-organisms without a simultaneous harmful effect on the normal cells of the host.

[1] Presented at a meeting of JYDSK MEDICINSK SELSKAB, January 25, 1948.
Submitted for publication, March 13, 1948.
Aided by grants from the Lady Tata Memorial Foundation and the Anders Hasselbalch Antileukemia Foundation.

Now it is a well-known fact that the cancer cell differs from the normal cells of the organism in certain fundamental qualities, which is manifested first of all in the uninhibited growth of the cancer cells in the organism. It is but natural to assume that the cause of the changed behaviour of cancer cells must be a qualitative change in the chemical structure of the cells and in the metabolic processes which take place in the living cells.

But in spite of an enormous amount of research work it has never, with certainty, been possible to demonstrate any chemical difference between cancer cells and normal cells. Such differences as have been found are of a quantitative nature. Generally the structure of cancer cells will approach that of normal undifferentiated cells. (This has been shown particularly with regard to their enzymatic pattern (GREENSTEIN).)

However, it is difficult to imagine that there should be no qualitative differences at all between the metabolic processes taking place in the cancer cells and those of normal cells. The only thing is that we do not know them, and accordingly we must so far be content with the possibility that they may be found some time.

If we knew such a difference, it would be feasible to carry on the search for chemotherapeutic agents against cancer on a far more rational basis than has hitherto been the case. At present this search must to a certain extent take place in the dark.

In consequence of this, American research workers have set out to test innumerable, widely different chemical compounds and groups of compounds. The substances are subjected to a so-called »screening», *i. e.*, their effects on animal tumours are investigated. If compounds are found, which seem to have an inhibitory action on the tumours, they are made the subject of closer investigations. Inter alia, a great number of derivatives are made in order to discover substances with more potent actions. These investigations are frequently conducted on a large scale and are typical examples of the much-talked-of American »team work».

We must be consoled by the fact that in the past, a successful therapeutic agent has been discovered before the actual nature of the disease has been recognized.

So far, however, the search for any substance which has a selective destructive action on malignant cells has not been successful. The effects of practically all chemotherapeutic agents of today are based on the fact that the so-called malignant cells are evidently more susceptible to damage than normal cells. This may in turn be due largely to the fact that the more rapidly cells proliferate the more vulnerable they seem to be.

The chemotherapeutic agents available at present are toxic substances which given in small doses inhibit or destroy the rapidly proliferating malignant tissue, but if they were to be given in such large doses that all the malignant tissue was destroyed, other tissues of the organism would be damaged to such an extent that it would be incompatible with the survival of the host. It would especially be the rapidly proliferating cells of the blood-forming organs, which would be damaged by such a procedure.

Yet, there may for all that be a possibility of discovering substances of this type, in which the margin between the therapeutic and toxic doses is sufficiently wide to make a cure possible. But it may be supposed that the chance is not very great. There seems to be a widely varying degree of resistance of the various cells in the same malignant process, so that the same tumour contains both easily destructible and comparatively resistant cells, at any rate so resistant that in this respect they equal the most sensitive among normal cells. Yet the conditions here are not quite clear.

As stated above, the action of such cytotoxic substances is manifested most plainly in the hyperplastic processes in the hematopoietic tissue. It is therefore also against such affections that substances have been discovered which have been employed in clinical work with some success.

Hence it is quite typical that it is just in these affections that chemotherapy has been known and used for many years. Arsenic, in the form of Fowler's solution, has been administered for leukemia since 1865 (LISSAUER). If arsenic is properly administered, it is capable of producing excellent remissions in chronic leukemia, particularly in the myeloid variety, with normalization of the white blood picture, increase of hemoglobin and the erythrocyte count, and regression of the hyperplastic processes. The same applies to benzene, which was first used in the treatment of leukemia in 1912 (KORANYI).

The action of benzene on the blood-forming organs is wellknown. Once benzene had been introduced into leukemia therapy, enthusiastic reports of cured patients appeared in the literature. Cure, in this respect, meant that at autopsy it was impossible to find traces of leukemic changes any more. The same holds good for the period following the advent of radiation therapy, for by this means it is possible to make the leukemic processes disappear almost completely, but only by such large doses that the patients are killed. That, however, does not imply that benzene cannot have an excellent palliative effect on leukemia when it is used with caution.

When the practical value of the new chemotherapeutic agents against leukemia is to be estimated, it is for the present necessary to look at their

palliative effect, and in the second place to see whether they are capable of prolonging the lives of the patients.

More particularly, it must be investigated to what degree a palliative effect can be obtained without at the same time inflicting injury to the normal hematopoiesis, and how long the duration of the palliative effect is before a new course of treatment is required.

Finally, the treatment must be compared with the results of such available methods as have so far been considered the best, *i. e.*, as far as leukemia is concerned, radiation therapy. Such an evaluation is, however, difficult and requires observations over a long period because of the many sources of error which, however, will not be discussed here.

Urethane

Urethane is one of the newer substances which has proved to be capable of affecting leukemia in such a way that the leukemic processes regress and the blood picture approaches normal.

The urethanes are esters of carbamic acid, so-called alkyl carbamates, and the substance passing under the name of urethane is actually ethyl urethane.

$$H_2NCOOC_2H_5$$

Urethane has been known for a long time. It has a narcotic effect, and has, inter alia been used for anesthesia of small experimental animals. For many years it has been known that urethane under certain conditions would influence cell division. I shall not embark upon describing the numerous investigations and observations which resulted in urethane being employed in the treatment of leukemia. Suffice it to say that urethane was first used experimentally against certain varieties of tumours in both animals and man. The effect on human tumours was slight, but the observation was made (EDITH PATERSON) that leukopenia would often develop in patients treated with urethane. Hence it was quite natural to test the action of urethane on leukemia, and it was observed that it produced a reduction of the number of leukocytes in leukemic patients with a simultaneous approach to a normal white blood picture. The first reports on those results appeared in the beginning of 1946 (PATERSON, THOMAS, HADDOW, and WATKINSON).

Since then scattered reports on urethane treatment of leukemia have been published. The practical value of the treatment is estimated rather differently, the series of patients are often very small, and as the treatment has been used only for about two years, the time of observation is as yet too short for final evaluation of the results.

However, it cannot be doubted that urethane is capable of influencing leukemic processes so that they regress to a certain extent, presumably through an inhibition of the mitosis in the hyperplastic leukemic processes. The effect is very pronounced in typical chronic myeloid leukemias. In favourable cases excellent remissions are obtained.

The leukocyte count falls steadily, the greatest diminution occurring in the most primitive cells, so that both a quantitative and a qualitative improvement of the white blood picture is achieved. The hemoglobin percentage and erythrocyte count increase and may reach fairly normal values, and the composition of the marrow is normalized, the size of the spleen is greatly reduced, the basal metabolism decreases, and what is very important, the general condition of the patients is also improved. Such a remission may now and again be just as pronounced as that following successful radiation treatment.

Generally the effect does not seem to be so good in the case of lymphatic leukemias, but also here it is possible, occasionally to initiate a good remission with decrease of glandular tumours and the size of the spleen, accompanied by improvement in the blood picture and general condition. However, a cure is definitely not obtained.

Urethane is administered by mouth in the form of tablets or in a solution to which a corrigent to improve the taste is added, but it may also be given per rectum or intravenously. The dosage varies greatly in the individual cases just as in radiation treatment. One should commence with small doses of 1—1.5 g by mouth daily increasing up to 4 or 5 grammes daily according to the effect and tolerance.

Frequently side-effects may be met with. Sometimes they are so pronounced that the treatment must be discontinued. The most frequent side-effects are nausea, vomiting, anorexia, and diarrhea. Furthermore, there is nearly always sleepiness and drowsiness owing to the narcotic effect of the drug. Many patients feel tired, and some complain of dizziness.

It is a palliative treatment, and it must be conducted on the same lines as radiation therapy, which means that one must aim at the greatest possible subjective improvement, at the same time avoiding damage to the hematopoietic tissue. The urethane treatment may give rise to agranulocytosis and development of »blast» leukemia just as in the case of too potent radiation and here it is of importance to know that frequently the effect will not be fully manifested until long time after the cessation of the therapy. This equally applies to treatment with roentgen, benzene, and urethane. Consequently at the Radium Centre we discontinue treatment when the number of leukocytes has fallen to one third of their initial number, irrespective of the effect otherwise obtained. A couple of months afterwards practically normal leukocyte

counts will often be found, at any rate in those cases treated by radiation. I shall not deal with the many contra-indications and danger signals, which may be of importance here. Suffice it to mention that the basal metabolism is often the best guide as to whether the therapy should be continued or not. This applies especially to the aleukemic varieties. As long as the basal metabolism is high at determinations made two or three times a week, there seems to be no risk involved in continuing the treatment.

Of course, there is no doubt that it is of exceedingly great theoretical importance that another substance has been found, which can effect the hyperplastic leukemic processes, but it is an open question how great a rôle it plays in clinical work so far. As mentioned above, there is some diversity of opinion as to this point. The effectivity must be compared with that of adequate radiation treatment.

In 1946 we treated 30 leukemia patients with urethane in the Radium Centre. All the leukemia patients of the year were treated with urethane. The material has been dealt with by Dr. BJERRE-HANSEN and will soon be published. I shall not enter into the details here, but just mention that our experiences may be summed up by stating that the effect of urethane on the chronic leukemias resembles the effect of radiation treatment, and that in some cases the urethane treatment may result in remissions which are just as good as those obtained by roentgen treatment, but that it is not the rule. Moreover, the individual remissions seem to be of a shorter duration and, on the whole, the side-effects seem to be somewhat more pronounced.

In my opinion urethane treatment does not constitute any great advance so far.

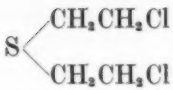
It has been shown that in mice and rats urethane may cause the development of adenomas in the lungs. Whether the same may be the case in man, has not yet been ascertained. This point may scarcely be regarded as a contra-indication in the treatment of leukemias since such tumours must be supposed to require several years for development.

In acute leukemias no definite effect of urethane has been obtained. In Hodgkin's disease urethane seems to have no effect either.

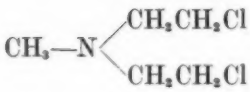
Nitrogen Mustards

Another group of substances which have proved to possess a marked cytotoxic action on rapidly proliferating cells is the so-called *mustard-gas compounds.*

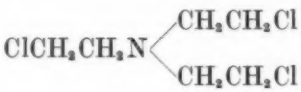
Mustard gas is a substance which is well-known from World War I. It made its appearance in 1917 and was used in gas warfare under the name of yperite. Chemically it is an alkyl sulphide.



Dichloroethylsulphide Yperite



Methyl-bis-(β-chloroethyl)amine



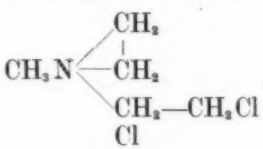
Tris(β-chloroethyl)amine

Also during the second World War extensive studies were made on the effect of mustard gas. Attempts were made partly to discover more active compounds, partly to find effective means of protection against mustard gas.

Accordingly, innumerable derivatives were produced, but information about their effect was, of course, kept secret during the war. The first publications on the biological effect of the various derivatives did not appear until after the war.

Among the derivatives which have been produced it is the so-called nitrogen mustards especially, which have been used in clinical experiments, more particularly the two compounds shown in Fig. 2.

The nitrogen-mustard compounds are alkylamines. In all essentials they have the same biological effects as the original mustard gas, but are more suitable for parenteral administration. The hydrochlorides are crystalline substances which are easily dissolved in sterile saline and may be given intravenously. The cytotoxic effect of these substances seems to be dependent on a cyclization, an intramolecular re-arrangement, with the formation of a cation and liberation of chloride ions (Fig. 3).



Applied locally they are vesicants. Several years ago this effect was successfully utilized in the treatment of skin tumours.

The resorptive effects of the various derivatives mentioned here are fairly uniform.

In lethal doses an effect on the central nervous system is obtained. There may be general convulsions and, in addition, cessation of respira-

tion. It may be supposed that a contributary cause of the cessation of the respiration is that the substances in question have an effect resembling that of curare producing muscular paralyses.

Given in sublethal doses the most serious changes will be found in the intestinal mucosa and in the blood-forming organs. In the course of a few hours it will be possible to observe the cytotoxic effect on the lymphatic tissue. There will be nuclear fragmentation and other signs of cell degeneration, followed by complete atrophy; also cytotoxic changes of the bone marrow, with various changes of the appearance of the cells, and gradually a complete cessation of the mitotic activity develops.

In many respects the effect resembles that of ionizing radiation. This resemblance also appears in other ways, and it is possible to induce mutations by mustard gas *e. g.*, in *drosophila* just as by roentgen radiation. In this respect the effect of mustard gases is more pronounced than that of any other drug investigated.

In 1942 GILMAN and PHILIPS began to treat a series of patients with various forms of neoplastic diseases with nitrogen mustards. In the first instance it was patients in the terminal phase of the diseases. However, no essential effect on the tumours was achieved, with the exception of a single case of lymphosarcoma.

These writers observed that during the treatment lymphopenia and neutropenia developed indicating inhibition of the leukopoiesis.

Experiments also showed that transplanted lymphosarcoma in mice regressed when the mice were injected with nitrogen mustards.

Later on various groups of investigators tried to treat hyperplastic diseases of the blood-forming organs (especially leukemias, polycythemia, Hodgkin's disease, lymphosarcoma, and myelomatosis) with nitrogen mustards.

These groups have now begun to publish some of their results, and with almost complete agreement report that it is possible to obtain a definite palliative effect particularly in Hodgkin's disease.

The affected lymphatic glands decrease in size; the temperature becomes normal; the pain abates, and sometimes the itching abates as well; the general condition may improve to a marked degree; and the basal metabolism may decrease.

The substances should be given intravenously. Perivenous injection may cause very untoward reactions. Doses of approximately 0.1 mg per kg body weight are generally given daily or every other day in series of 5—6 injections.

Administered in these doses nitrogen mustards generally induce a number of toxic symptoms, partly acute symptoms from the gastro-

intestinal canal, and partly signs of damage of the blood-forming tissue, which appear after the lapse of some time.

The acute symptoms appear a few hours after the injection. Almost invariably the patient feels nauseated, and there is often vomiting, lasting for some hours. In addition, there is often diarrhea.

The unavoidable side-effects from the hematopoiesis will also appear fairly soon. In the first place, a lymphopenia develops, later on the granulocyte and platelet counts also decreases. On the other hand, the effect on the erythrocyte count is generally slight, probably because of the much greater longevity of the erythrocytes.

However, the sensitivity of the hematopoietic system varies with the individual, and therefore hematological examinations must be carried out very carefully during the treatment.

When the drug is withdrawn, regeneration of the hematopoiesis starts again remarkably soon in contradistinction to what is the case in roentgen treatment where regeneration comes much slower.

If the course of treatment is repeated, it seems as though the tendency to leukopenia becomes greater each time, even if the leukocyte count between the courses may reach normal values.

It is not a question of curing Hodgkin's disease. Nitrogen mustards are toxic to all cells, but the action on rapidly proliferating cells is very marked. Therefore the aim is to find a dose producing the greatest possible effect on the abnormally proliferating cells without simultaneous irreparable damage to the host.

The remissions in Hodgkin's disease are often of fairly short duration. On the whole, they seem to be of much shorter duration than those obtained by roentgen radiation, and most of the larger groups of investigators admit that nitrogen-mustard therapy is not superior to roentgen radiation. Nevertheless, we may meet with cases resistant to roentgen treatment, in which some favourable effect has been obtained by nitrogen mustards, and some of these cases have become sensitive to radiation treatment again. However, it is not always quite clear what is understood by »resistant to roentgen treatment», and in addition roentgen therapy is administered in different ways in different institutions.

In my experience nitrogen-mustard therapy in Hodgkin's disease has a special field of indication. It sometimes happens we are confronted with a patient suffering from Hodgkin's disease apparently without localized processes. However, the patient is ill and highly uncomfortable from an excruciating itching which is so frequent in this disease. This generally means that somewhere in the organism there is an active process of Hodgkin's disease, though we are unable to localize it.

In such cases practically nothing can be done by means of roentgen,

but sometimes an excellent result may be achieved with nitrogen mustards.

On the whole it seems most rational to use the nitrogen mustards in the more generalized cases, which often at the same time will be the late cases, and not in the localized easily accessible types. It is too early to pronounce on combined therapy. This is still in the experimental stage, and one must proceed with great care in such a combination.

Nitrogen mustards also seem to have an excellent effect on polycythemia. However, there may be reasons for being a little reserved. Patients with polycythemia may live for many years, and, we do not know the late effects of the nitrogen mustards, but bearing in mind its capability of inducing mutations and its peculiar effect on the cells, it is not unreasonable to assume that the substance may prove cancrogenic.

In the chronic leukemias nitrogen mustards will now and then produce remissions resembling those of radiation treatment. Here, too, the remissions seem to be of shorter duration, particularly in the lymphatic leukemias.

In the acute leukemias there has been a doubtful effect in some cases. But it is difficult to judge the effect here because spontaneous, complete remissions, lasting several weeks, may be encountered.

There is some diversity of opinion as to lymphosarcoma. In certain cases a fairly good palliative effect has been achieved.

A fairly good result seems also to have been achieved in some cases of mycosis fungoides.

A striking palliative effect has been observed in cases of anaplastic bronchogenic carcinoma. However it must be remembered, that even a slight diminution in size of the tumour in such cases will often relieve the patient of his symptoms to a marked degree (*e. g.* in comparison to the same diminution of a mammary tumour).

Stilbamidine

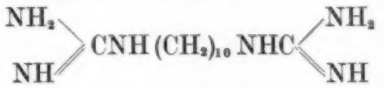
Finally I want to mention a chemotherapeutic agent which differs from all the others by influencing the growth of one certain type of cell only. It is stilbamidine, the effect of which seems selectively directed against the myeloma cells in myelomatosis.

As will be known, in myelomatosis (multiple myeloma) a diffuse or localized tumourous hyperplasia of cells of the plasma-cell type in the bone marrow is found, accompanied by peculiar changes in the serum proteins, the most frequent being a hyperproteinemia caused by a

hyperglobulinemia. The sedimentation rate is consequently very high. In many cases there is Bence-Jones protein in the blood and urine.

The development which resulted in the action of stilbamidine being tried on myelomatosis is rather remarkable.

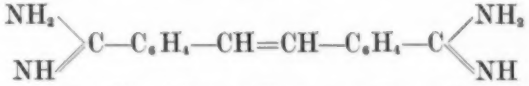
Trypanosomes require glucose for survival on a nutrient medium. Since the trypanosomes cannot survive without glucose, experiments were made, in which trypanosomiasis was treated with drugs producing a reduction of the blood sugar (JANSCÓ and JANSCÓ, 1935). Among others, synthalin was tried, and it proved that synthalin did have a definite therapeutic action on mice infected with trypanosomes.



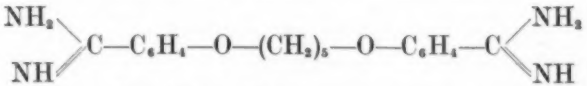
Synthalin

However, it was shown that the therapeutic action was not related to the action on the blood sugar, *e. g.*, insulin has no influence upon trypanosome infections, and synthalin has a trypanocidal effect in vitro.

These observations led to the study of drugs with trypanocidal effect, and a large number of compounds were investigated with a view to their trypanocidal action. More active compounds were found, of which the following two have become important:



4 : 4 diamidino stilben = stilbamidine



4 : 4 diamidino dibenzoxypentane = pentamidine

These substances have proved very valuable in the treatment of patients infected with Leishmania donovani, *i. e.*, suffering from kala-azar.

In kala-azar — as in myelomatosis — changes of the protein content of the serum with hyperglobulinemia are met with, and on this slender analogy SNAPPER began in 1945 to treat patients with myelomatosis with stilbamidine and pentamidine.

Once more it was demonstrated that wrong assumptions may lead to positive results, for while stilbamidine did not influence the abnormal protein conditions in myelomatosis patients, it seemed nevertheless to have a favourable symptomatic effect.

It was emphasized especially that the patients were relieved of their

pain. This is of great importance, as severe bone pain is an outstanding symptom of myelomatosis. In SNAPPER's opinion the effect is so pronounced that the patients must be kept in bed for some time to prevent them from moving too early and too freely in order to avoid spontaneous fracture.

Later on, recalcification took place in some cases, but on the whole, the osteolytic processes remained unchanged as far as may be judged from the roentgenograms, but the progress of the disease seemed to be arrested, at any rate for some time.

Last year I had an opportunity of going through some of SNAPPER's cases with him in the Mount Sinai Hospital in New York, where I saw a number of the patients, and I can testify that in many of them pain had disappeared in a surprisingly short time, and the processes in the bones seemed to have been retarded in their development.

Yet, a cure was not obtained. Pathological changes in the sternal marrow and in the serum proteins persisted.

During treatment certain cytologic changes occur in the myeloma cells, evidenced by the presence of basophilic granules in the cytoplasm, while similar changes do not occur in any of the normal cells of the bone marrow. These granules seem to be the result of a direct action of stilbamidine on abnormal proteins in the cytoplasm of the myeloma cells.

Since the action thus appears only on the myeloma cells, the possibility exists that here we have a chemotherapeutic agent with a fairly specific effect in a neoplastic affection.

In the Radium Station we have treated some myelomatosis patients with stilbamidine, so far only six.

As recommended by SNAPPER, stilbamidine was administered intravenously in doses of 150 mg (after a smaller test dose), daily, in some cases only every other day, totalling 15 injections in a series. Stilbamidine should be injected immediately after it has been dissolved.

The injections are given slowly, but nevertheless they may cause a marked fall in the blood pressure, and if one is not very careful, even collapse. Therefore adrenaline must always be at hand. These disagreeable vasomotor reactions may be almost completely prevented if atropine sulphate is given before the stilbamidine injection.

During the treatment the patients must be placed on a diet poor in protein, otherwise there seems to be no effect on the myeloma cells. The cause is not quite clear, but it is believed that stilbamidine participates in the metabolism of the myeloma cells instead of certain amino acids, which must therefore not be given in too great a quantity.

In addition to the acute side-effects some late complications may appear. In a fairly large number of the cases anesthesia occurs in the area of distribution of the trigeminal nerve some months after a series

of stilbamidine injections: it is a dissociated anesthesia with preserved sensation of pain, but very discomforting to the patients. This neuropathy is probably due to toxic degeneration of the principal sensory nucleus of the trigeminal nerve. In the six patients we have so far treated this anesthesia was very marked in two and weaker in a third case, *i. e.*, in one half of the series.

The anesthesia will persist for many months, but is reported to disappear again.

It is maintained that the other substance in question, pentamidine, does not cause this anesthesia to the same extent, but so far we have been unable to obtain this drug.

Our own experiences with stilbamidine confirm that in some cases an astonishing effect is obtained on the patients' pains. In the course of 2—3 weeks two patients, who were unable to get out of bed unaided, were up and could move around reasonably freely, one of them, at any rate, quite unimpeded. In other patients too the analgetic effect has been very favourable.

On the other hand, our experiences also corroborate that in no case has there been a normalizing effect, neither in the sternal aspirations, nor in the protein content of the serum. Nor has it been possible, with certainty, to demonstrate any recalcification of the bone lesions, and in one case — a patient with a so-called solitary myeloma in the spinal column — a generalization with foci in the ribs and myeloma cells in the sternal marrow appeared for the first time during treatment. Stilbamidine, too, evidently affects the normal bone marrow, for the number of erythrocytes was generally reduced in our patients, and a leukopenia repeatedly developed during the course of treatment.

It is difficult to predict at present the practical importance of the stilbamidine treatment. Sufficient time has not yet elapsed. As already stated a cure for the disease is not obtained, but the possibility of discovering more effective compounds exists in this condition too.

It is difficult to imagine that there should be any profound effect on the myelomatous process when the abnormal protein conditions in the serum are not changed at all, for these conditions must indeed be indicative of the extent and intensity of the processes.

Closing Remarks

In conclusion I may mention that in addition to the chemotherapeutic agents discussed here we know of other groups of compounds with a different chemical structure, which have also proved capable of affecting the abnormally rapidly proliferating growth of cells, but their investigations have not yet reached an advanced stage. However, these

problems are studied very intensely in cancer research, of which leukemia research is a branch.

It may be said that the clinical results so far achieved do no encourage any optimism, as in most cases it is possible by other methods to obtain equally good results, indeed, very often even better results.

Yet, from a theoretical point of view these substances represent great achievements, and the optimism is due to the fact that by the discovery of all these different compounds it may be possible to find new compounds with a more selective effect on the abnormally proliferating cells which will have a greater therapeutic action and yet avoid the toxic effect on normal tissue.

At the same time we learn from these substances a great deal about the chemical processes upon which growth, differentiation, and division of cells are based. This is very important since, as said above, a really effective chemotherapy of cancer must surely be based on qualitative differences of the vital processes which must exist between normal cells and the so-called malignant cells.

SUMMARY

In a survey of the chemotherapy of hyperplastic disorders in the blood-forming organs it is emphasized that the effect of the present-day chemotherapeutic agents is based on the fact that the so-called malignant cells are more susceptible to damage than normal cells, which in turn seems to have a certain relation to their rapid proliferation. Most »anti-neoplastic» chemotherapeutic agents are toxic substances with a special influence on cell division, which explains their inhibiting action on the growth of the rapidly proliferating malignant cells. However, in order to obtain a complete inhibition of all malignant tissue of a diseased organism, it would be necessary to administer such large doses of the toxic substances that the most rapidly proliferating normal tissue, and the hematopoietic tissue in particular, would also be damaged to a degree which is incompatible with survival of the host. The ideal chemotherapeutic agent must surely be based on a real qualitative difference between malignant and normal cells, but we do not yet know such differences.

Urethane, nitrogen mustards, and stilbamidine are then discussed in detail.

ZUSAMMENFASSUNG

In einer Durchsicht der Chemotherapie hyperplastischer Störungen der blutbildenden Organe wird betont, dass der Effekt der heutigen chemotherapeutischen Wirkstoffe auf dem Umstand fusst, dass die sog. malignen Zellen gegen Schädigungen empfindlicher sind als normale Zellen, was seinerseits mit ihrer raschen Wucherung in gewissem Zusammenhang zu stehen scheint. Die meisten »anti-neoplastischen» chemotherapeutischen Wirkstoffe sind toxische Substanzen mit besonderem Einfluss auf die Zellteilung, was erklärt, dass sie das Wachstum der rasch wuchernden malignen Zellen hemmen. Die Erzielung einer vollständigen Hemmung aller malignen Gewebe eines erkrankten Körpers würde jedoch die Verabfolgung so grosser Dosen der toxischen Substanzen erfordern, dass auch die am schnellsten wuchernden normalen Gewebe

und ganz besonders die blutbildenden Gewebe so stark geschädigt würden, dass es mit einem Überleben des Wirtsorganismus nicht vereinbar wäre. Der ideale chemotherapeutische Wirkstoff muss sicherlich an einem wirklichen qualitativen Unterschied zwischen malignen und normalen Zellen angreifen, doch ist uns solch ein Unterschied bisher nicht bekannt. Darauf werden Urethan, Senfgas und Stilbamidin näher besprochen.

RÉSUMÉ

Dans un aperçu consacré à la chimiothérapie des désordres hyperplastiques des organes hématopoétiques l'auteur souligne que l'effet des agents chimiothérapiques actuels est basé sur le fait que les cellules dites malignes sont plus susceptibles d'être endommagées que les cellules normales, ce qui à son tour semble tenir, dans une certaine mesure, à leur rapide prolifération. La plupart des agents chimiothérapiques «anti-néoplasiques» sont des substances toxiques ayant une influence spéciale sur la division cellulaire, ce qui explique qu'ils inhibent la croissance des cellules malignes à prolifération rapide. Cependant, pour obtenir une inhibition complète de tout tissu malin d'un organisme malade il serait nécessaire d'administrer des doses si fortes de ces substances toxiques que le tissu normal dont la prolifération est la plus rapide, et le tissu hématopoétique en particulier, en seraient lésés à un degré incompatible avec la survie du sujet. L'agent chimiothérapeutique idéal doit certainement avoir pour base une véritable différence qualitative entre cellules malignes et cellules normales, mais jusqu'ici nous ne connaissons point pareille différence. Ensuite, l'auteur soumet à une discussion détaillée l'uréthane, les moutardes nitrogènes et la stilbamidine.

FROM THE KING GUSTAF V's JUBILEE CLINIC IN LUND, SWEDEN
(CHIEF: B. EBENIUS, M. D.)

DEPTH DOSE MEASUREMENTS IN THE ESOPHAGUS IN ROENTGEN ROTATION THERAPY[1]

by

Kurt Lidén

The roentgen rotation method was introduced at the King Gustaf V's Jubilee clinic in Lund in 1942 by EDLING (1) and later improved by the present head of the clinic B. EBENIUS. The results obtained indicated that in treating esophageal cancer the range of permitted variation of the total central depth dose is very narrow. Hence an accurate determination of this dose is of decisive importance.

The theory of the depth dose distribution in the rotation method has been fully treated by DU MESNIL DE ROCHEMONT (2—7). However, accurate theoretical calculations of depth doses are extremely difficult for the following reasons:

a) The shape of the cross-section of most parts of the human body is not easily susceptible to mathematical calculation.

b) The different body tissues have widely differing powers of absorption.

c) There are great differences between individual patients.

d) It is sometimes difficult to keep the object of the treatment, in this case the esophageal cancer, coincident with the rotation centre because of movements of the patient.

Certainly, the errors of the theoretical calculation may greatly exceed the permitted margin for esophageal cancer. Hence the demand for clinical reasons, for an instrument with which to measure accurately the central depth dose in the esophagus.

Apparatus consisting of condenser chambers contained in an ordinary rubber sound proved unsuitable because of the thickness of the walls of the sound. Finally the apparatus described below was evolved. It has given satisfactory results since 1944 and meets the clinical requirements of small dimensions, flexibility, and reliability. A cylindrical

[1] Submitted for publication, March 24, 1948.

a. b.

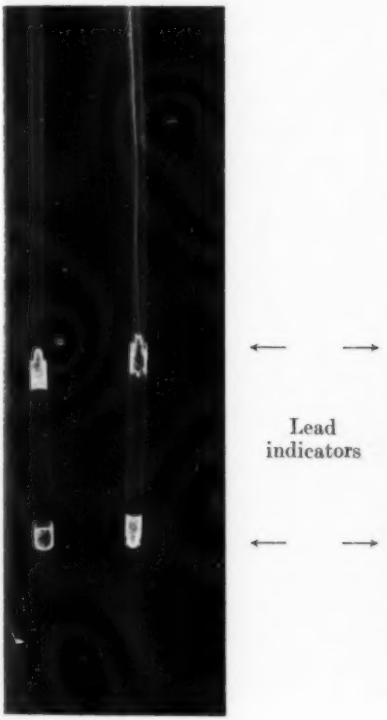


Fig. 1. Fig. 2.

Fig. 1. A roentgenogram of the two forms of instrument for central depth dose measurements in a) the esophagus, b) in the lower part of the throat.
Fig. 2. A roentgenogram of the instrument in the esophagus of a patient.

capsule of aluminium is mounted on an esophageal bougie nr. 16; the outer diameter of the capsule is 6 mm and its wall thickness only 0.2 mm, forming a container for two cylindrical condenser chambers, each 20 mm long and 5 mms diameter (external measurements) as described by SIEVERT (8). The capsule is closed by means of a greased threaded stopper; a little paper packing keeps the two chambers in contact and prevents them from moving in the capsule. The bougie is of soft material and is screwed into the end of the aluminium capsule which has been previously threaded. As an additional precautionary measure, a metal wire is soldered to the capsule, drawn through the bougie, and fixed to the upper end of the bougie (see Fig. 1). In order to make it possible

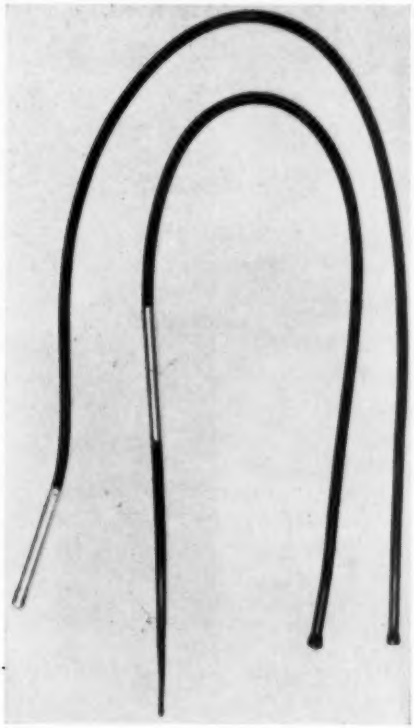


Fig. 3. The two types of instrument complete.

to observe on a fluorescent screen the location of the capsule in the esophagus, a small lead indicator is enclosed in each end of the capsule. Fig. 1 a shows a roentgenogram of the instrument; Fig. 2 is a roentgenogram of the same instrument in the esophagus of a patient.

A variant of the equipment has appeared suitable for measuring the central depth dose in the lower part of the throat (Fig. 1 b). In this case, to be sure that the capsule is centrally situated, the bougie has been divided 10—15 cm from its lower end and the capsule mounted between the two parts. The lower, shorter, part of the bougie is introduced into the esophagus and thus holds the apparatus in a suitable central position. Fig. 3 shows both forms of the instrument.

It may be noted in passing that NICOLAEFF and THORAEUS (9) have recently described experiments with a plastic sound.

The cylindrical condenser chambers used in this investigation were

specially manufactured in order to permit of accurate measurements of the normal central depth dose, about 200 r. For calibration they were enclosed in the capsule, which was placed between and in contact with two paraffin blocks, each having a thickness of 10 cm and a diameter of 30 cm. A secondary standard ionization chamber of the type described by THORAEUS (10) was placed between the same paraffin blocks in a position corresponding to that of the capsule in the radiation beam. Booth the capsule and the ionization chamber were then simultaneously irradiated.

The results indicate that the voltage drop or response of the chambers in the paraffin wax, which corresponds to the chambers being in an esophagus, is somewhat greater than the voltage drop of the chambers in surface dose measurements using the same radiation quality. The average increase in this voltage drop is 6 % and is of course due to the secondary radiations set up in the paraffin wax or human tissue. This increase in voltage drop will vary from patient to patient according to their different physical structures; but such individual variations will be relatively small, certainly much less than 6 % of the total voltage drop. Hence measurements and calculations of the central depth dose on different patients, using the same chambers and with unaltered constants, should introduce an error much smaller than 6 %. This error is certainly smaller than the ordinary observation error of condenser chamber measurements, *i. e.* 2—3 %. The quality of radiation used, was of course the same as in the clinical treatment viz. 165 kV D. C. with a filter of 0.5 mm Cu + 1 mm Al (H. V. L. 0.85 mm Cu).

In Lund, central depth dose measurements are regularly performed in roentgen rotation therapy of esophageal cancer by means of the above described apparatus, which in its present form works very well.

SUMMARY

A special instrument for measurements of the central depth dose in roentgen rotation therapy of esophageal cancer is described. The main part is an aluminium capsule fixed to an esophagus bougie. When in use two specially calibrated cylindrical condenser chambers are placed in the capsule. A variant for measurements in the lower part of the throat is also described.

ZUSAMMENFASSUNG

Es wird eine besondere Apparatur beschrieben zur Messung der Herd-Dosis bei Röntgen-Rotationsbehandlung von Krebs der Speiseröhre. Ihr Hauptteil besteht aus einer an einer Speiseröhrensonde befestigten Aluminiumhülse. Zwei besonders kalibrierte Kondensatorkammern werden in der Hülse angebracht. Auch eine Abart zur Messung in der unteren Partie des Rachens wird beschrieben.

RÉSUMÉ

Description d'un appareillage spécial pour mesurer la dose focale dans le traitement du cancer de l'oesophage aux Rayons Roentgen par la méthode rotatoire. Sa partie principale est constituée par une capsule d'aluminium fixée à une bougie oesophagienne. Deux chambres d'ionisation calibrées de façon particulière sont placées dans la capsule. L'auteur décrit aussi une variante pour la dosimétrie au niveau de la partie inferieure du pharynx.

REFERENCES

1. Edling, L., Acta Radiol. *25*, 427, 1944.
2. du Mesnil de Rochemont, R., Strahlenther. *60*, 648, 1937.
3. » » » » » *66*, 593, 1939.
4. » » » » » *68*, 221, 1940.
5. » » » » » *69*, 407, 1941.
6. » » » » » *71*, 512, 1942.
7. » » » » » *72*, 121, 1943.
8. Sievert, R., Acta Radiol. *15*, 197, 1934.
9. Nicolaeff, A. and Thoraeus, R., Acta Radiol. *28*, 776, 1947.
10. Thoraeus, R., Acta Radiol. *18*, 471, 1937.

FROM THE ROENTGEN DIAGNOSTIC DEPARTMENT OF KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN (CHIEF: PROF. ÅKE ÅKERLUND)

FURTHER STUDIES OF THE INTERURETERIC RIDGE OF THE BLADDER[1]

by

Nils P. G. Edling

In Acta Radiologica XXII (1941) the writer has described the aspect of the interureteric ridge on the cystogram and pointed out the practical value of its study for location of distal ureteric concretions, and changes of the bladder base. KERR and GILLIES (1944) in their monography write, on the contrary, that they have not found it of any value in the diagnosis of either calculi or tumors. However, the daily experience of the routine during the following years has argued in our favour. For demonstration, the author has put together 135 urographies, consecutively performed on as many patients with symptoms of ureteral calculi, and studied the appearance of the interureteral ridge.

In order to be visible in the cystogram the interureteric ridge must be anatomically adequately developed in the base of the bladder, and a good roentgen technic also must be used.

Anatomically there is a ridge stretching transversely across the bladder, between the folds on whicb the ureters open into the bladder (Fig. 1). In the cystogram the intermediate part appears most markedly; therefore the writer terms the formation the interureteric ridge and encloses the ureteric folds, as well. The interureteric ridge is generally more prominent in men than in women, and may be hypertrophied by longstanding obstacle to the outflow from the bladder (trigonal bar). The ridge that separates the trigone from the retroureteric fossa is flattened if the bladder is greatly distended.

The interureteric ridge is best studied on urography. A moderate degree of bladder filling offers the most accuracy — as in examination of the bladder in general. If the bladder is evacuated just before the beginning of the examination it acquires an adequate degree of filling and opacity

[1] Submitted for publication March 2, 1948.

about half an hour after the intravenous injection of the contrast medium. The radiographs must be heavily exposed. A very important point is the projection. The antero-posterior axis of the bladder is inclined some degrees in caudo-cranial direction, a direction of the central ray in consequence is necessary for viewing the base of the bladder tangentially. The interureteric ridge is therefore best seen if the central ray is adjusted caudo-cranially in supine position. The common frontal view in 15—20 degrees cranio-caudal adjustment is usually not adequate (Fig. 4).

The antero-posterior view of the contrast-filled normal bladder shows a distinct bowed contour that is continuous and cranially concave (Fig. 2). It is symmetrical as to shape and position. The lower ends of the ureters always run caudally of this contour transversing the bladder wall. The distance between the ureteral contrast and the contour is 2—3 mm. Cranially of the interureteric ridge the bladder has its greatest density, due to the fact that the bladder here has its largest antero-posterior depth, and to the sedimentation of the contrast medium to that part of the lumen in supine. In lateral view the interureteric ridge sometimes is visible as a small bulging into the bladder base a short distance behind the internal urethral opening. The great opacity of the subject's body in this projection makes the location difficult and a study of details is not possible.

In the pathological cases that have a swelling of the intramural part of the ureter there is an asymmetrical interureteric ridge and a greater distance than normal between the terminal part of the ureter and the contour of the ridge, The affected side may have a cranially convex course instead of the normally concave or may be more raised than normal (Figs. 3—5, 7). Or, the contour is visible only on the pathological side and has an altered shape (Fig. 6).

In the 135 patients that belong to the material of the writer the bladder examinations on urography were performed not only with 15—20 degrees cranio-caudal adjustment of the central ray but also with vertical or to some degrees caudo-cranial projection. In this routine material the contour of the interureteric ridge was visible in 77 of the cases, that is in a few more than a half.

In 37 (32 male + 5 female) of these cases there was a concretion in one of the ureters near the opening into the bladder. The same side of the interureteric ridge had a cranially convex curve or a more raised course than the other side, indicating swelling of the wall of the intramural part of the ureter. This swelling is an important and hitherto not enough observed indirect sign of a calculus. Due to the increased prominence of the interureteric ridge of the affected side the ridge may be visible already in the cranio-caudal projection, also. This fact makes it possible to study the change of the position of a suspicious calculus or concretion-like shadow in relation to the ridge, and in that manner determin-

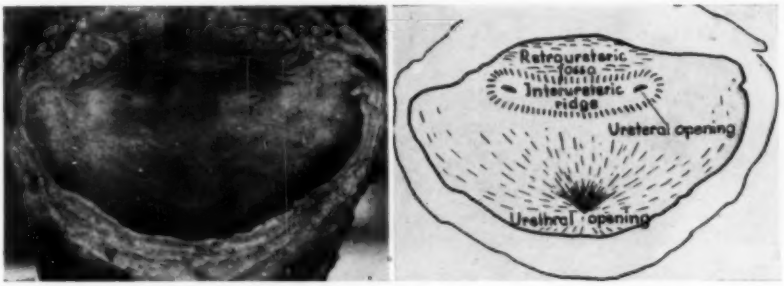


Fig. 1. Specimen. The base of the bladder showing the internal urethral orifice, the trigone, the ureteral openings on the interureteric ridge, and the retroureteric fossa.

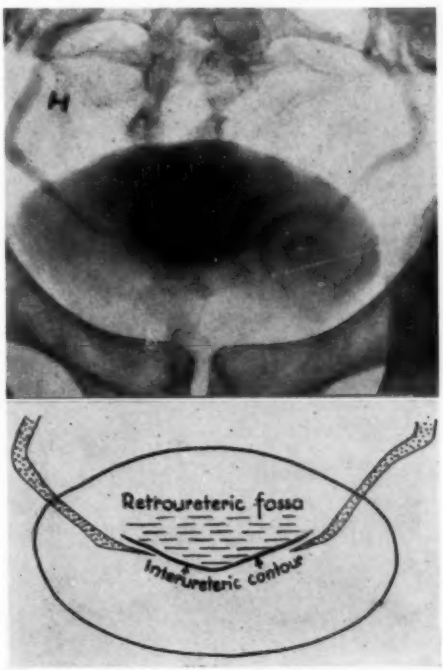


Fig. 2. Normal case. The interureteric ridge is visible as a symmetric, bowed contour concave in cranial direction. The intramural parts of the ureters run caudally of the contour. The retroureteric fossa appears with the greatest opacity.

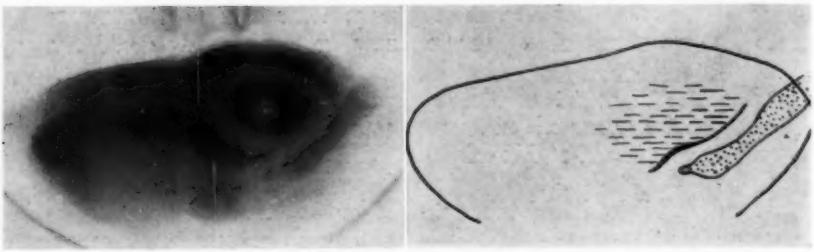


Fig. 3. Left-sided concretion with asymmetric interureteric ridge and stasis.

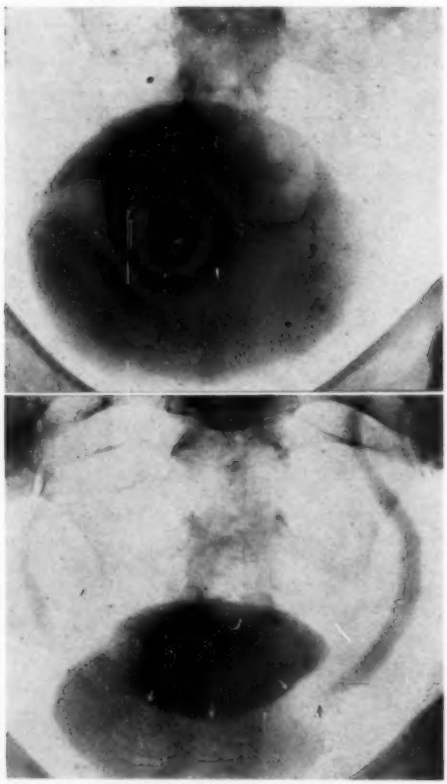


Fig. 4 a.

Fig. 4 b.

Fig. 4. Left-sided concretion with slightly asymmetric interureteric ridge indicating swelling. The ridge is visible only in true antero-posterior projection (b), not in cranio-caudal (a).

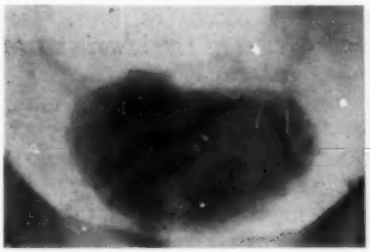


Fig. 5.

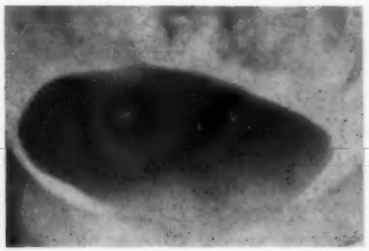


Fig. 6.

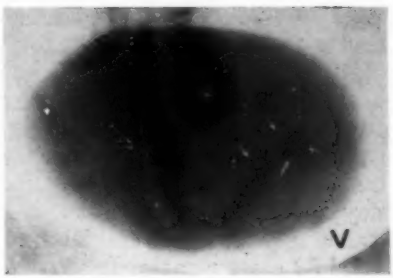


Fig. 7.

Fig. 5. Concretion on the left side with oblique interureteric contour and pronounced stasis. Contrast urine only from the healthy kidney and ureter.

Fig. 6. Interureteric contour only visible on the left side, cranially convex, indicating swelling of the intramural part of the left ureter one hour after a calculus has gone. No stasis.

Fig. 7. Asymmetrical interureteric ridge due to a leftsided concretion without stasis. Probably, the calculus causes a dilation of the intramural ureter only, but no swelling of the wall.

whether this shadow belongs to the ureter or is located outside of it. The study of this point is of special importance if the function of the kidney is so decreased that no contrast filling of the ureter above the concretion appears. The contrast urine from the healthy kidney still makes the study of the interureteric ridge possible. In 13 of the 37 cases no contrast filling of the lower part of the ureter had appeared after 30 minutes of examination, neither in 7 of these 13 cases after more than 50 minutes of observation. By locating the suspicious calculus to the lower end of the ureter with help of the interureteric ridge, it is in many cases possible to shorten the time of examination and makes awaiting the contrast filling for location and diagnosis unnecessary. In 5 of the 37 cases one could by a urography performed earlier or later see a nor-

mal interureteric ridge with symmetrically bowed contour, cranially concave. Then the concretion was not present in the lower end of the ureter.

The interureteric ridge was also visible in 34 cases (30 male + 4 female) in which the concretion was present in the ureteral lumen outside of the bladder wall, that is cranially of the ridge. In all these cases the cystograms showed a normal interureteric contour.

In the remaining 6 cases (4 male + 2 female) with visible interureteric ridge no opaque calculus could be seen. In 4 of these — 2 with stasis — the interureteric ridge showed signs of swelling on the same side as other symptoms. In one of the cases with stasis there was no visible contrast filling of the actual ureter after 55 minutes of examination but the contrast urine from a double ureter of the same side, and from the healthy ureter made it possible to study the ridge. — In both of the cases without stasis the concretion had gone, so far as can be judged, and the asymmetry of the interureteric ridge was caused by a remaining swelling. — In the remaining 2 of the 6 cases no asymmetry was seen. One of them showed a stasis in the ureter cranially of the intramural part. In the second the excretion of the kidney was retarded at least one hour, probably due also to a transparent calculus in the more cranial part of the ureter.

Of the whole material 58 cases remain. In these cases the contour of the interureteric ridge was not visible. In 10 of them (8 male + 2 female patients) an opaque calculus was present in the lower end of one of the ureters, with stasis in 9 cases, without in one. In spite of the presence of a concretion no roentgenological sign of swelling could be demonstrated in these cases. 46 cases (31 male + 15 female) had the concretions cranially of the intramural part, 45 with stasis, one without. The last 2 cases (1 male + 1 female) had transparent calculi with stasis.

Conclusions. By urography one should not neglect to study the appearance of the interureteric ridge, with a proper technic. In several cases of calculus in the intramural part of the ureter the interureteric ridge shows a swelling that is an important indirect sign of concrement, complementary to other symptoms. In cases with total obstruction on the affected side it is possible to study the interureteric ridge with help of the contrast urine from the healthy kidney. In that way, one can localize an opaque concretion in relation to the interureteric ridge even then the ureter is not contrast filled. If the one side of the interureteric ridge is swollen and no concretion is visible, the finding indicates a transparent calculus, or a calculus having recently passed the ureteral opening.

SUMMARY

The writer describes the aspect of the interureteric ridge in the cystogram on urography and points out the practical value of that study in the diagnosis of ureteral concrements. The investigation bases on a routine material of 135 cases.

ZUSAMMENFASSUNG

Der Verfasser beschreibt das Aussehen des Interureterwulstes im Röntgenbilde bei Urographie und weist auf den praktischen Nutzen dieses Studiums für die Diagnose von Uretersteinen hin. Die Untersuchung baut auf ein Routinematerial von 135 Fällen.

RÉSUMÉ

L'auteur décrit l'aspect de la crête interurétérale sur le cystogramme pratiqué au cours de l'urographie et signale l'importance pratique de cette étude pour le diagnostique des calculs urétéraux. Ce travail se base sur une série de 135 cas.

BIBLIOGRAPHY

EDLING, NILS P. G., Der Interureterwulst im Röntgenbild, Acta radiol. 22: 573, 1941.
KERR, H. DABNEY & GILLIES, CARL L., The urinary tract (Chicago: The Year Book Publishers, 1944).

FROM THE KING GUSTAF V's JUBILEE CLINIC IN LUND, SWEDEN
(CHIEF: B. EBENIUS, M. D.)

THE INTENSITY DISTRIBUTION OF THE 2 GR TELERADIUM UNIT OF THE KING GUSTAF V's JUBILEE CLINIC IN LUND[1]

by

Kurt Lidén

In 1945 the teleradium unit at the Jubilee clinic in Lund was completely rebuilt in accordance with a design described recently by BENNER (1). The 40 tubes, each containing 50 mg of radium element, were distributed along two concentric circles in a circular container in order to permit the use of a conical lead-tungsten filter according to BENNER (2) (Fig. 1). The container was attached to the end of a steel ribbon wrapped around a motor-driven lead wheel; rotation of this wheel transports the container from its protected position to the nozzle of the unit, *i. e.* to the position shown in fig. 1. This movement takes about 5 to 6 seconds. Similarly the container may be moved from the nozzle to the protected position. The protection afforded in the protected position in all directions is equivalent to a thickness of 10 cm of lead. In treating a patient, the mouth of the unit is adjusted to the desired location and then the motor moving the radium container is started from the control room. Simultaneously a synchronous electric clock is automatically started, the clock having been previously adjusted to the actual treatment time. When the radium container has reached the correct position a switch automatically stops the motor driving the lead wheel. At full treatment time a switch in the clock starts the movement of the radium container to the protected position. In the event of a failure in the electrical supply, the clock stops but the radium container remains in the nozzle; this may cause unknown errors in the treatment time. To prevent this happening, an additional relay is mounted; this relay starts a mechanically-operated reserve clock, when the main supply is interrupted. When the mains voltage returns, the reserve clock stops and the teleradium unit again works normally. This system permits an exact deter-

[1] Submitted for publication, March 24, 1948.

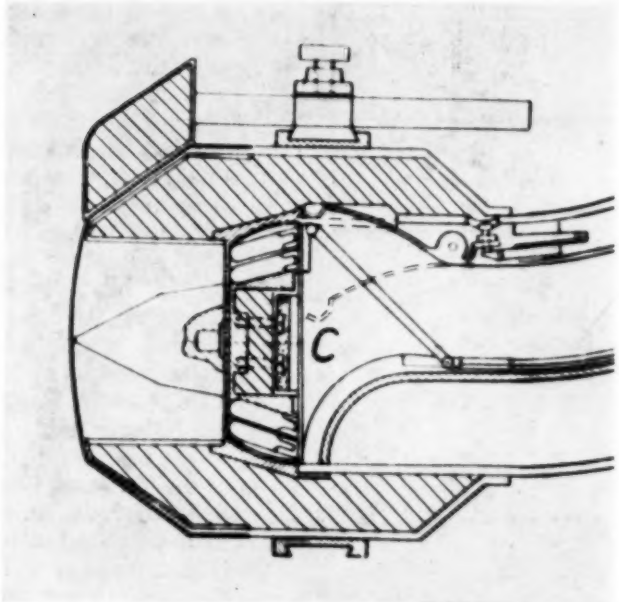


Fig. 1. The nozzle of the teleradium unit with the radium container C in treatment position. (From BENNER (1).)

mination of the treatment time under all circumstances and prevents an unintentionally incorrect dosage being administerred.

At the rebuilding of the teleradium unit, clinical considerations suggested that, if possible the treatment times should be relatively short without any appreciable decrease of the relative depth doses. According to BENNER (3) the use of an extra filter, equivalent to 3 mm lead in the 3 gr teleradium unit in Stockholm, caused a smaller relative depth dose than for the original 2 gr unit in Lund, where no extra filter was inserted. At the re-investigation, now necessary, of the intensity distribution of the new unit in Lund with the somewhat decreased radium-skin distance (41 mm), it was decided to check this conclusion.

The intensity measurements were performed by means of spherical condenser chambers according to SIEVERT (4). For this purpose a paraffin-wax phantom, composed of two cylindrical blocks, each with a diameter of 26 cm and a thickness of 10 cm, were used. The curved surface of each block was flattened at one point (Fig. 2). One side of each block was made accurately flat; in this accurately flat side of each block

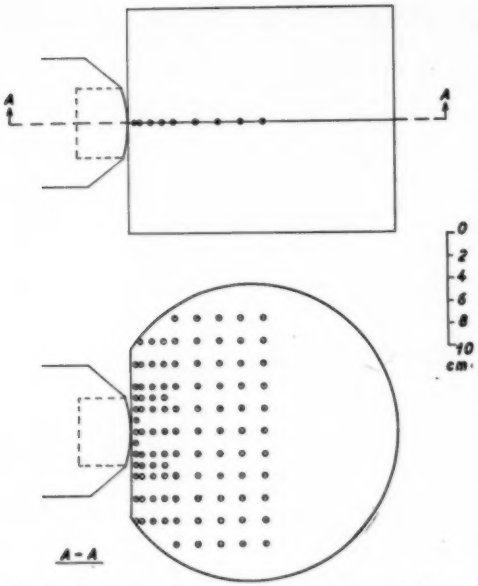


Fig. 2. The paraffin-wax phantom used in the intensity measurements of the teleradium unit. The positions of the condenser chambers' centre are indicated with small circles. The contour of the nozzle is shown to the left.

a row of hemi-spherical hollows was made with specially constructed borers. The row was arranged to be perpendicular to the main direction of irradiation. In the hollows of one block, condenser chambers with an external diameter of 10 mm were placed. The accurately flat surfaces of the blocks were placed together, the hemispherical hollows in each block being exactly opposite each other. This row of hollows was then irradiated. When measurements were complete this row of hollows was filled up and a second similar row was made in a parallel but lower position. This was repeated to a depth of 12 cm. The surface intensity was examined by means of needle chambers according to BENNER (5). They were readily put at my disposal by the Radiophysical Institute of King Gustaf V's Jubilee clinic, Stockholm. In the region 0 to 4 cm from the surface of the unit the time of exposure reached such small values that a correction had to be applied to allow for the irradiation of the chambers before the radium container had reached its final position. The correction was calculated by taking a series of measurements at the same distance but with different times of exposure.

Complete measurements were performed in the following three cases: a) without any extra filter, b) with a conical filter only, and c) with a 3 mm lead filter but with no cone. The results in the cases a) and b) appear in the isodose diagrams of Fig. 3. The surface intensity measured was in a) 91 Imc, in b) 66 Imc and in c) 71 Imc. (Imc = the intensity at 1 cm distance from a point source of 1 mg Ra filtered by 0.5 mm Pt, corresponding to about 8 r per hour.) In case b) the surface intensity of the re-built unit was slightly greater than that of the original unit (with cone); at the same time the new unit gave a negligible decrease of relative depth intensity. In case a) a small increase of the relative depth

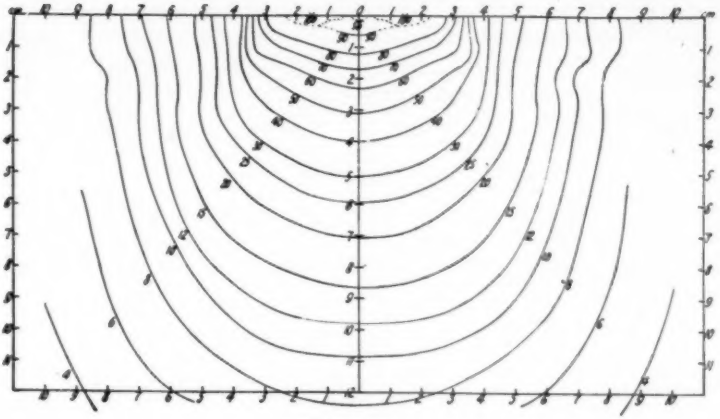


Fig. 3 a.

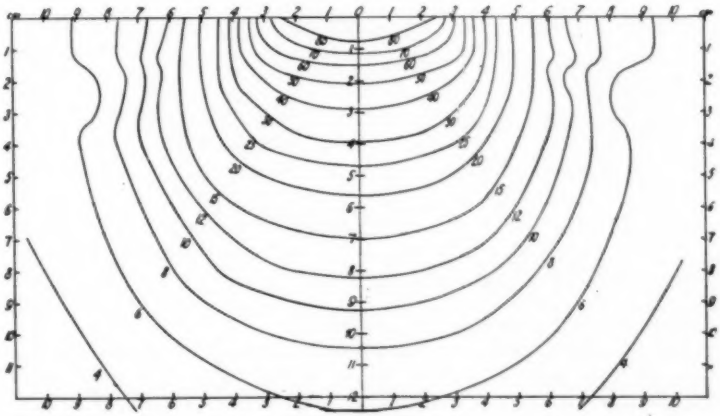


Fig. 3 b.

Fig. 3. Isodose diagram for the teleradium unit, a) with lead-tungsten cone (max. surface intensity 66 Imc), b) with no lead-tungsten cone (max. surface intensity 91 Imc).

intensity was obtained. In case c) the 3 mm lead filter gave no definite improvement of the relative depth intensity as compared with the results obtained without a filter. For that reason an extra filter is never used in the clinical treatments.

The operation of this new teleradium unit in Lund and the clinical results obtained have both been satisfactory. The reliability in running

is good. The distribution of the radium and the distance radium—skin have given intensities and relative depth doses which allow such treatment times as are desirable from the clinical point of view. Without the cone a surface dose of 1000 r is obtained in 82 minutes and with the cone in 113 minutes.

SUMMARY

The intensity distribution of the rebuilt 2 gr teleradium unit of the King Gustaf V's Jubilee clinic in Lund has been measured. Isodose diagrams are given. Experience has shown the automatic mechanism to be reliable in operation and the instrument gives good clinical treatment times.

ZUSAMMENFASSUNG

Es wurde die Intensitätsverteilung bei dem umgebauten Teleradiumapparat der Jubiläumsklinik König Gustav des V. in Lund untersucht und Isodosendiagramme gezeichnet. Die Erfahrung lehrt, dass die automatisierte Apparatur betriebssicher ist und vorteilhafte klinische Behandlungszeiten gibt.

RÉSUMÉ

On a étudié la répartition de l'intensité obtenue avec l'appareil à Téléradium après sa reconstruction, à la Clinique Jubilaire du Roi Gustave V à Lund, et l'on a établi des diagrammes d'isodoses. L'expérience montre que l'appareil rendu automatique est d'un fonctionnement sûr et permet des temps d'irradiation avantageux dans son emploi clinique.

REFERENCES

1. Benner, S., Acta Radiol. *28*, 765, 1947.
2. —, Acta Radiol. *18*, 297, 1937.
3. —, Acta Radiol. *18*, 873, 1937.
4. Sievert, R., Acta Radiol. *Suppl. 14*, 1932.
5. Benner, S., Acta Radiol. *15*, 291, 1934.

FROM THE I. ROENTGENDIAGNOSTIC DEPARTMENT OF SÖDERSJUKHUSET, STOCKHOLM, SWEDEN (CHIEF: DOCENT G. JÖNSSON).

IN COOPERATION WITH THE II. MEDICAL CLINIC OF SÖDERSJUKHUSET, STOCKHOLM (CHIEF: PROFESSOR G. NYLIN), AND THE SURGICAL CLINIC OF SABBATSBERG'S HOSPITAL, STOCKHOLM (CHIEF: PROFESSOR CL. CRAFOORD)

VISUALIZATION OF PATENT DUCTUS ARTERIOSUS BOTALLI BY MEANS OF THORACIC AORTOGRAPHY[1]

by

G. Jönsson, B. Brodén, H. E. Hanson and J. Karnell

Patent ductus arteriosus is a malformation localized entirely within the mediastinum. It can therefore be examined roentgenologically only by methods of contrast roentgenography. Ever since the introduction of angiocardiography about ten years ago, large series of congenital defects have been subjected to examination by means of this method. STEINBERG, SUSSMAN & GRISHMAN, however, seem to have compiled the most extensive observations of angiocardiography in cases of patent ductus. In an article published in 1943, these authors reported 27 cases of patent ductus examined by means of angiocardiography. In a »Discussion of Angiocardiography and Angiography» published in 1947, SUSSMAN & GRISHMAN summed up their experiences as follows:

»Practically all cases of this condition which we have studied with the aid of angiocardiography revealed an abnormality in the outline of the aorta, not encountered in normal individuals or in other cardiac abnormalities, consisting of an apparent localized dilatation of the descending aorta on its anterior aspect just beyond the isthmus. The changed segment varies in size and shape from a localized bulge to a uniformly dilated segment. This appearance is probably due in most cases to the infundibulum of the ductus, although occasionally it may represent a traction aneurysm of the aorta caused by the ductus. The appearance, however, is not pathognomonic. Traction on the aorta from any cause will produce the same abnormality.

Because in the presence of a patent ductus, blood is shunted from the aorta to the pulmonary artery or its left branch, it was anticipated that the ductus itself might be visualized or that there might be prolonged or renewed visualization of the pulmonary arteries. Neither expectation has been realized; on rare occasions a vascular structure has been seen which might have been the ductus proper, but its position in a maze of other vascular structures prevented identification. Prolonged or renewed visualization

[1] Submitted for publication, June 15, 1948.

of the pulmonary artery was seen in a few cases, but the slight change in the density o this structure was no greater than might be present in any series of roentgenograms an the finding was therefore interpreted with caution. Presumably, clear visualization i impossible because the contrast medium in the pulmonary artery becomes too dilute when it is reshunted through the ductus.»

Accordingly, the above-mentioned authors have demonstrated a practically constant anatomic change (infundibulum or traction aneurysm) in patent ductus arteriosus which they, nevertheless, do no consider as pathognomonic. They were unable to visualize the ductus proper, nor was any shunting of contrast blood from the aorta to the pulmonary artery definitely ascertainable. Also FURMAN has presented a case of patent ductus with visualization of a »traction aneurysm» in the aorta. CHAVÈZ, DORBECKER & CELIS, who at angiocardiography inject the contrast medium through a catheter inserted through the right jugular vein and the superior vena cava into the right auricle, have reported a case of patent ductus arteriosus where renewed visualization of the pulmonary artery was obtained »at the time that the aorta fills», stating this to be »a decisive radiologic sign; it is only possible if there is a fistulous connection between the two vessels.» Still, it must be considered highly doubtful whether renewed visualization of the pulmonary artery is pathognomonic of patent ductus arteriosus. Renewed visualization with considerably more marked density in the left main branch of the pulmonary artery is, of course, indicative of patent ductus (proceeding to the left main branch), but a general renewed visualization may appear even in the case of other left to right shunts. It is difficult to distinguish clearly when this starts in a series of pictures. It is, therefore, no doubt impossible to decide whether an observed renewed visualization is due to patent ductus arteriosus or, for instance, to a ventricular septum defect localized high up.

Angiocardiography offers good anatomic information about the right chambers of the heart and the pulmonary artery. In these parts of the circulation, the contrast medium is still concentrated enough to make the contours distinctly visible. When the contrast passes through the pulmonary section of the circulation, the dilution increases to such an extent as to render the opacity in the left chambers and in the aorta too faint for detailed examination. This applies to adults. At angiocardiography in children a comparatively larger quantity of contrast medium can be used thus diminishing the effect of the dilution. The method employed by CHAVÈZ et al., with injection into the right auricle through a catheter, may conceivably give rise to a more satisfactory concentration of the contrast medium, in view of the fact that the dilution at this mode of procedure begins in the heart and not, according to the usual method in the peripheral veins. This may serve to explain why these authors

record a distinct renewed visualization in their case of patent ductus arteriosus. Another drawback of angiocardiography, of even more significance than the dilution with regard to a study of the aorta, and that particularly complicates the diagnosis of patent ductus, may be mentioned here. When the opacity has reached its maximum in the aorta, there is still so much opaque substance left in the pulmonary vessels that the outlines of the aorta become difficult to distinguish. For the same reason, it is also hard to discern a pathological communication between the aorta and the pulmonary artery and it is impossible to decide whether this communication is a patent ductus arteriosus or an interarterial communication with a different localization.

Thus, merely from a theoretical point of view, angiocardiography may be considered to be an unsuitable method for the examination of patent ductus arteriosus. Furthermore, as already mentioned in the introduction to this article, practical experience will corroborate this. At contrast roentgenography in cases of interarterial communication between the aorta and the pulmonary artery, the contrast medium should be injected into the aorta. CASTELLANOS & PEREIRAS (1939) demonstrated the possibility of filling the aorta descendens in children with contrast medium by injection in a retrograde direction into the left brachial artery (*counter-current aortography*). In this way, they were able to disclose a patent ductus arteriosus. However, according to our own experience, this method cannot be applied to adults. Methods of *aortography after puncture* of the aorta ascendens through the sternum (NUVOLI 1936, RADNER 1945) or parasternally through the second left interspace (DEL CAMPO & HOYOS 1946) must, on account of the risk of complications (*e. g.*, pneumothorax, mediastinal emphysema, pericarditis), be regarded as less suitable. The above-mentioned authors have not reported any single case of patent ductus that was examined by means of this method.

In an article presented in this Journal in 1948 we described two cases of coarctation of the aorta and one normal case examined by a method for *thoracic aortography by catheterization from the radial artery.* We maintained that this method, suggested by RADNER (1948) and modified by us[1], is preferable to that of angiocardiography at contrast roentgenography of cases of coarctation of the aorta and patent ductus arteriosus, as well as of other malformations in the aorta and its intrathoracic branches. We have used this method in two cases of patent ductus and in one case of another interarterial communication that proved of great

[1] A method for *angiography of the abdominal aorta by catheterization* has been described by FARIÑAS (1941): The femoral artery is exposed and punctured with a trocar through which the catheter is passed.

interest from a differentialdiagnostic point of view. The same *technique* has been applied as in the coarctation cases, except that the catheter was introduced so far into the aorta ascendens as to bring the tip of it close to the orifice. The value of this technical detail will be discussed in connection with the case reports. In another case of patent ductus, the examination was not a success owing to the fact that the catheter could not be inserted as far as the aorta, probably because of some malformation in the right subclavian artery.

Case Reports

Case 1. Married woman, aged 26, with slowly progressing troubles from dyspnea at exertion and palpitation for the last six to seven years. *Phys. exam.:* Prolonged, continuous thrill and typical continuous murmur in the 1st left intercostal space. *Blood pressure:* 120/65—60. *ECG:* Normal position of electrical axis. *Roentgen exam.:* Moderately enlarged heart (volume per square meter of body surface = approx. 500 cc). The pulmonary conus bulging more than usual, otherwise no definitely pathological shape. Central pulmonary vessels wide.

Clin. diagnosis: Typical case of patent ductus arteriosus.

Aortography: The catheter was inserted through the right radial artery with the tip lying in the anterior sinus of Valsalva. Contrast injection (50 cc of a 70 % diodrast solution) was performed after the first picture had been taken. In the following series of pictures, the contrast is seen to fill the aorta ascendens and the arcus aortae as well as the pulmonary artery, particularly its left branch. Between the upper part of the aorta descendens and the pulmonary artery, an opacified vessel is observed — patent ductus arteriosus. No other communication between the great vessels is noticed (Figs. 1—4).

The sinus of Valsalva and the coronary vessels are visualized.

Aortographic diagnosis: Patent ductus arteriosus proceeding to the left branch of the pulmonary artery.

Operation (CRAFOORD); *Double ligature of patent ductus arteriosus.* The ductus is 9 mm in diameter and 4—5 mm long. Continuous thrill, not particularly marked.

Case 2. Storekeeper, aged 47. Rheumatic infection in childhood. From that time a diagnosis of heart disease. All through life, dyspnea after exertion, generally in connection with palpitation, and irregular pulse. For the last two years, increasing decompensation troubles with leg edema.

Phys. exam.: Circ. organ: Moderate cyanosis. Dyspnea at every movement. Peripheral edema. *Heart:* Systolic + diastolic murmur with maximum in 3rd left intercostal space. The murmurs cannot be definitely stated to be continuous in character. Regular rhythm. *Blood pressure:* 125/75. *Venous pressure:* 23 cm. *Decholin time:* 40—60—70 seconds. *ECG:* Right axis deviation + auricular preponderance.

Fig. 1.

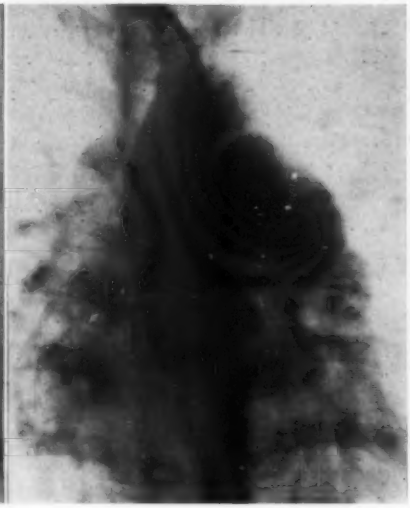


Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

Roentgen exam.: Considerable enlargement of all parts of the heart (volume per square meter of body surface = approx. 1,100 cc). Greatly widened pulmonary artery and central vessels in the lungs. The peripheral vessels in the lungs are widened aswell.

Blood gas analysis by heart catheterization: right auricle — 9 vol % O_2, right ventricle — 10.4 vol % O_2, pulm. artery — 14.3 vol % O_2.

Discussion: The blood gas analysis indicates a considerable mixture of arterial blood in the pulmonary artery. The difference occurring between the right auricle and the right ventricle may be explained by a pure relative insufficiency of the pulmonary valves.

Summary: A patient, aged 47, with interarterial communication that had given rise to right heart failure. The clinical picture differs from the usual one in cases of patent ductus arteriosus by, inter alia, 1) the lack of a continuous murmur, 2) enlargement of the right part of the heart with right axis deviation in the ECG.

Clinical diagnosis: VOC congenit. (D. arteriosus persistens? + Insuff. valv. pulmonalis? + Incomp. cordis.

Aortography: The catheter is inserted through the right radial artery. Its tip lies in the ascending aorta near the semilunar valves. 50 cc of a 70 per cent diodrast solution is injected in the course of 10 seconds. In the first picture, taken when half the quantity of contrast matter had been injected, the contrast is seen to fill the aorta and the left branch of the pulmonary artery. In a lateral view, between the pulmonary artery and the upper part of the aorta descendens, opaque substance is observed within a large area, indicating a broad interarterial communication (Fig. 5).

The sinus of Valsalva are sharply outlined. The right coronary artery is filled with contrast medium.

Aortographic diagnosis: Large patent ductus arteriosus proceeding to the left branch of the pulmonary artery.

Operation (CRAFOORD); *Division of ductus arteriosus + suture of aorta and art. pulm.* The communication was a patent ductus, the thickness of a thumb and only a few mm long. No continuous thrill was noted.

In this case, an interarterial communication between the aorta and the pulmonary artery was ascertained by blood gas analysis after catheter examination of the heart. However, the diagnosis of patent ductus

rteriosus could not be established owing to the atypical clinical obser-ations otherwise (no continuous murmur). Aortography served to con-irm the diagnosis and, by visualizing the ductus proper, showed this o be very wide.

Case 3. Artist, aged 26. Heart disease ascertained by school doctor. Entirely ree from subjective symptoms with the exception of slightly affection when performing tlethics during the last few years.

Phys. exam.: Heart: Pulsations over the pulmonary artery. Strong continuous thrill nd murmur in 2nd left intercostal space, though the systolic component predominates ver the diastolic one more than is usual in cases of patent ductus arteriosus. *Blood pres-ure:* 140/55. *Venous pressure:* 9 cm. *ECG:* Left axis deviation, otherwise no pathological igns.

Roentgen exam.: The heart made large pulsations, as also the aorta and the left hilus. Heart volume per square meter of body surface = approx. 700 cc. Left cardiac contour bulging more than usual. Since the pulmonary artery is not particularly dilated, the deformity of the left contour may conceivably be due to an enlargement of the left ventricle, though an enlargement of the right ventricle may cause a similar deformity. The central lung vessels are widened.

Blood gas analysis: Increase in the oxygen saturation in the pulmonary artery of the venous blood from 10.4—12.8 vol. % O_2, which corresponds to a shunting of 50 per cent of the aorta blood through the interarterial communication. The mean pressure in the pulmonary artery is but insignificantly increased.

Discussion: The character of the murmur does not entirely correspond to conditions at a *typical* patent ductus.

Clin. diagnosis: Interarterial communication.

Aortography: Catheter through the right radial artery to the aorta ascendens. The tip of the catheter is lying 5 cm from the semilunar valves. The first picture was taken before the contrast injection had started. In the second picture, only a slight amount of contrast is noticed in the aorta, but an increased density is seen in the region of the pulmonary truncus. In later pictures, contrast filling is observed in all parts of the pulmonary artery. The opacity of the aorta is faint throughout the picture series.

Aortographic diagnosis: Interarterial communication between the aorta and the pulmonary artery, possibly localized near to the base of the heart.

Operation (CRAFOORD); *Exploratory thoracotomy:* Patent ductus arteriosus was not to be noted. The pulmonary artery was very wide. Its main branch had the appearance of a fusiform aneurysm, where the thickest part of the spindle lay about halfway between the region of the valves and the point of issue of the pulmonary artery from the pericardium. A typical continuous thrill, of the same kind as generally felt over a patent ductus arteriosus, was restricted to a small area within the conus nearest to the valves.

Probable diagnosis: Ruptured aneurysma of the sinus Valsalvae.

This is a very interesting case from the point of view of differential diagnosis. An interarterial communication was ascertained at blood gas analysis between the aorta and the pulmonary artery, but the continuous murmur was not typical of patent ductus. At aortography in this case, the first striking observation was the slight opacity in the aorta. As a rule, good opacity is obtained in the aorta when the tip of the catheter lies close to the valves and the injection is performed rapidly, both these conditions being fulfilled in this case, and also when there is no reason to suspect aortic incompetence. Further, at the aortography an increase in the density of the pulmonary truncus was noticed at an early stage, that was of only a small degree and insufficient for demonstration in reproductions but, nevertheless, distinct enough to suggest that contrast matter had passed over from the aorta to the pulmonary artery. Both these phenomena, viz. the slight opacity in the aorta and the increase in the density of the pulmonary truncus at an early stage of the contrast injection, are fully explained by the observation made during the surgical intervention of an interarterial communication localized close to the origin of the great vessels. The injected contrast substance is instantly distributed between the aorta descendens and the dilated pulmonary artery, and the opacity in the aorta therefore becomes less than usual. — Since aortographic findings, of the kind met with in this case, have not been ascertained previously, we did not venture to make any definite statements regarding the localization of the interarterial communication. However, the observations made are of indisputable significance. Cases of this type cannot be operated upon and, if the interarterial communication can be localized by means of aortography, exploratory thoracotomy becomes superfluous.

Conclusions: The following observations have been made in two cases of *patent ductus arteriosus* by means of thoracic aortography:

1) *Contrast substance passed over from the aorta to the pulmonary artery.* In both cases, the left main branch of the pulmonary artery and its ramifications were the most opacified.

2) *The interarterial communication was a patent ductus arteriosus.* The ductus proper was opacified, but not sufficiently clearly outlined to permit detailed observation. Still, it was possible in both cases to obtain a reliable conception of the width of the ductus.

No infundibulum or traction aneurysm, such as SUSSMAN & GRISMAN, and others, observed at angiocardiography, has been visualized in our cases of patent ductus.

In one case with an *interarterial communication near the origin of the great vessels*, phenomena were manifested that differed entirely from those of patent ductus arteriosus.

In our opinion, thoracic aortography should be resorted to before operation in established cases of patent ductus arteriosus. Also in cases where the clinical diagnosis is definite, it is of great value for the surgeon to obtain as detailed anatomic information as possible before the intervention. We hope to develop our technique in thoracic aortography so as to render possible a determination of the length and width of the ductus in cases of patent ductus by means of this method, these facts being of particular importance to the surgeon.

SUMMARY

An account is given of two cases of patent ductus arteriosus and of one case of interarterial communication with another localization, examined by means of thoracic aortography.

ZUSAMMENFASSUNG

Bericht über zwei Fälle von offenem Ductus arteriosus Botalli und einen Fall von Verbindung zwischen Aorta und Art. pulm. mit anderer Lokalisation, die mittels thorakaler Aortographie untersucht wurden.

RÉSUMÉ

Description de deux cas de persistance du canal artériel de Botal et d'un cas de communication entre l'aorte et l'artère pulmonaire avec autre localisation, examinés à l'aide de l'aortographie thoracale.

REFERENCES

Brodén, B., Hanson, H. E. and Karnell, J.: Thoracic aortography. — Acta Radiol. 29: 181 (1948).

Castellanos, A. and Pereiras, R.: Counter-current Aortography. — Revista Cubana de Cardiología. Vol. 2: 187 (1939).

Chavèz, I., Dorbecker, N. and Celis, A.: Valor diagnostico de los Angiocardiogramas obtenidos por Inyeccion directa intracardíaca a través de una Sonda. — Arch. del Instit. de Cardiología de Mexico. Vol. 17: 121 (1947).

—, Direct intracardiac angiocardiography — its diagnostic value. — Am. Heart Journal 33: 560 (1947).

Del Campo, C. G. and Hoyos, J. M.: Angiography of the aorta. — Summary of a communication. Am. Heart J. 33: 729 (1947).

—, Angiography of the thoracic aorta and coronary vessels with direct injection of an opaque solution into the aorta. — Radiology 50: 211 (1948).

Fariñas, P. L.: New technique for the arteriographic examination of the abdominal aorta and its branches. Am. J. Roentgenology. 46: 641 (1941).

FURMAN, R., A.: Angiocardiography: Its use in the diagnosis of patent ductus arteriosus. — The New England J. of Med. 238: 116 (1948).

NUVOLI, I.: Ref. in Zbl. f. Radiologie 22: 382 (1936).

RADNER, S.: An attempt at the roentgenologic visualization of coronary blood vessels in man. — Acta radiol. 26: 497 (1945).

Thoracal aortography by catheterization from the radial artery. Acta radiol. 29: 178 (1948).

ROBB, G. P. and STEINBERG, I.: A practical method of visualization of the chambers of the heart, the pulmonary circulation and the great vessels in man. — Journal Clin. Investigation 17: 507 (1938).

STEINBERG, M. F., GRISHMAN, A. and SUSSMAN, M. L.: Angiocardiography in congenital heart disease. III. Patent ductus arteriosus. Am. J. Roentgenol. 50: 306 (1943).

SUSSMAN, M. L. and GRISHMAN, A.: A discussion of angiocardiography and angiography. Advances in Int. Med. Vol. II: 102 (1947).

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT OF THE UNIVERSITY CLINICS
IN LUND, SWEDEN (CHIEF: PROF. H. HELLMER)

RUBBER CASSETTE WITH INTENSIFYING SCREENS DESIGNED FOR ROENTGEN EXAMINATION OF OPERATIVELY EXPOSED ORGANS[1]

by

Olle Olsson

The roentgen examination of an operatively exposed kidney is an old method that was initially documented in the literature in 1907 (HEINEKE). One of the reasons why this procedure was first adopted was the difficulty inherent in the production of plain renal radiograms distinct enough to be of value in the establishment of a detailed diagnosis. A direct radiological examination of the exposed organ rendered a better control of the scattered radiation possible and reduced the time of exposure, resulting in a better contrast and sharpness. The progress made in roentgen technique since the introduction of this method has however considerably improved the quality of radiograms, and thereby, as far as the above reasons are concerned, mitigated the necessity of the method in question.

Today this method answers another purpose, namely, to facilitate the location of calculi in a kidney exposed for operative treatment, and to check whether the removal of the stones is complete. It had been observed in many a material that the frequency of so-called recurrences of renal calculi after operative treatment was astonishing. The obvious explanation of such recurrences was that calculi or stone fragments had been overlooked at operation and thus escaped removal. The most important conclusion drawn from this assumption was obviously that the kidney must be roentgen controlled during the operation in order to determine the possible presence of residual stones or fragments.

In the radiological examination of the operatively exposed kidney it has hitherto been the rule to use films without intensifying screens. The film package was generally prepared separately as occasion arose. A suitably sized film was wrapped in ordinary black paper and then

[1] Submitted for publication, April 8, 1948.

packed in a sheet of rubber, a sterilized operation sleeve or the like. Special cases have also been designed for this purpose, *e. g.* that used by PFLAUMER. ÅKERLUND standardized the method in a simple manner. He had ready-packed films made similar to those employed in dentistry. These films are now supplied by all the leading film manufactures. A ready-packed film of this type is placed in a sterilized rubber glove. In order to prevent infection when the packed film is being introduced into the glove, use is made of a loading guide, consisting of a metal sleeve. The whole package is then held against the exposed kidney by means of elastic ribbons.

Thanks to this standardization of the method kidney roentgen control has been facilitated considerably.

For this examination ordinary cassettes (JACHES, FRANÇOIS etc.) or thin cassettes made specially for the purpose (BENJAMIN, PUIGVERT GORRO) have also been used. As these cassettes are stiff, it has however been difficult to introduce them into the operation wound, besides which they had to be wrapped in a sheet of rubber or the like in order to prevent infection.

The employment of a cassette rendered the use of intensifying screens possible, whereby the contrast was intensified and the exposure time considerable reduced.

In an endeavour to combine the advantages inherent in the utilization of a flexible, small, conveniently packed film and those made available by the use of intensifying screens, the writer has designed a rubber cassette similar to that employed in industry for the roentgen inspection of material. The cassette consists simply of a flat rubber bag 10 × 15 cm. (Fig. 1 a).[1] The film and two intensifying screens are dropped into the bag. The mouth of the bag is closed by means of a clamp. The bottom of the bag is provided with a spout through which the air content of the closed bag may be withdrawn by means of a syringe. This decreases the thickness of the cassette and at the same time presses the screens tight against the film.

The screens are of the type used for industrial purposes. They are supplied in standard sizes such as 9 × 12 cm., 10 × 24 cm., and 10 × 48 cm. These screens are characterized by the fact that the fluorescent coating has been applied to a flexible material.

Thanks both to the material of the cassette and the construction of the screens the loaded cassette is very flexible (Fig. 1 b). In this manner we have *an easily sterilizable, convenient and flexible cassette with intensifying screens.* The cassette has been dimensioned to suit a standard

[1] Trelleborgs Gummifabriks AB, were courteous enough to manufacture rubber cassettes of the above mentioned type.

Fig. 1 a. The rubber cassette.

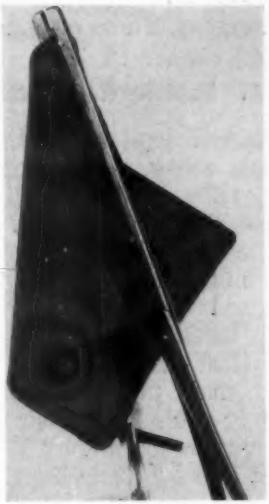


Fig. 1 b. Cassette closed and air withdrawn. Picture shows flexibility of the cassette.

sized film 9 × 12 cm. As mentioned further up standard screens, coarse and fine-grained, are available for this size of film.

The rubber cassette is sterilized in the same manner as the rest of the rubber articles used at operation. An assistant with sterilized gloves holds up the sterilized cassette in the dark room of the operation department, where it is loaded with the aid of a guide consisting of a metal sleeve (ÅKERLUND). The mouth of the cassette is closed by the assistant with a single pair of resection tongs or with two, one on either side. The mouth may also be closed in any other suitable manner. If tongs are used, such types should be chosen as may be used as handles when the cassette is being introduced into the operation wound. When loaded the cassette is placed on the assistant's table and the air withdrawn. Every time the syringe is removed from the spout, the latter is closed by means of a clip. As a rule, about 60 cc. air can be sucked out of the cassette. When the air has been withdrawn the spout is sealed by means of a small stopper. The cassette is then ready for use. It is immaterial which of the screens is placed next to the organ to be examined. To render the double-sided use of this cassette possible the practice of making one of the sides of the cassette of lead rubber, for example, to prevent secondary radiation from the underlayer, has been discarded.

Experiments have shown that this type of cassette is suitable especially for two particular methods in the radiological examination of exposed organs. These procedures will be described in the following.

A. Radiological examination of operatively exposed kidneys

The radiological examination of an exposed kidney may be made by fluoroscopy or radiography. Fluoroscopy is far inferior to radiography (BEER, ÅKERLUND). If a radiogram of the organ is to be made, the cassette may be placed outside the operation incision (SUTHERLAND, ASTRALDI and URIBURN) or it may be inserted in the actual wound and lie in immediate contact with the kidney. Strictly speaking, the first mentioned type of examination does not fall within the scope of the present method. This discussion refers exclusively to the latter type of radiological examination of the exposed kidney.

The main purpose of the radiological examination of an exposed kidney is to check whether the removal of the calculi is complete before an operation for kidney stones is terminated, but the method is indicated also for disclosing the presence and location of calculi. Furthermore, it is sometimes discovered that stones appearing as integral units in the plain radiogram consist in reality of several small calculi. FRANÇOIS always injects air into the renal pelvis when performing a radiological examination of the exposed kidney and thus produces a gas pyelogram. HEUSSER suggests also an inter-operative pyelogram with positive contrast medium.

The use of guide needles has been proposed in the locating of possible calculi (QUINBY, PETRÉN) or a grid (PUHL, UEBELHÖR etc.).

Experience has shown the method to be of considerable value. In a paper published in 1937 ÅKERLUND gives, inter alia, a report of experiences made by this examination method. Its value has been confirmed further by later publications. PFLAUMER & FRIEDRICH, for example, say in their short monograph »Gang und Technik der Röntgenuntersuchung auf Harnsteine» 1940: »Ganz unerlässlich ist aber die Röntgenphotographierung bei jeder Nierensteinoperation.» In 1942 MAY writes; »Nach eigener Erfahrung .... unbedingtes Bedürfnis ... die freigelegte Niere .. darstellen zu können.» PRIESTLEY (1938) and OPPENHEIMER (1940) assert that operative roentgen control is a valuable aid in the operative treatment of renal calculi. On the basis of a comprehensive experience PUIGVERT GORRO (1943) writes: »Die direkte Roentgenaufnahme der Niere während der Operation verdient eine weitere Verbreitung und sollte ohne Einschränkung in allen urologischen Stationen angewendet werden.»

The dissonance in this chorus of praise of the method in question

even of late years is however that due to its mention in KNEISE and SCHOBER's book »Die Röntgenuntersuchung der Harnorgane» 1941. These authors contend that its adoption is unnecessary.

At the Surgical Clinic, Lund (Head Prof. J. P. STRÖMBECK) the radiological examination of the exposed kidney is the rule in the operative treatment of renal calculi. This examination is a link in a system necessary for obtaining as detailed a knowledge as possible of the results of an operation for renal calculi. The pre- and interoperative roentgenological examination of renal calculi ought to comprise the following steps:

1. Plain radiograms of the urinary tract and excretion urography, if necessary, complemented by retrograde pyelography.
2. In those cases to be operated on and in which one suspects that the stones might have shifted, plain radiograms of the urinary tract are taken immediately before operation.
3. Radiological examination of the exposed kidney in every case, at least before the termination of the operation.
4. Complete radiological examination including excretion urography, before the patient is discharged from hospital.

A very important step in the above schedule is the radiological examination of the exposed kidney. We have hitherto adopted the technique recommended by ÅKERLUND. In spite of the fact that a good roentgen instrumentarium is at our disposal, the long exposure time sometimes resulted in vague radiograms with poor contrast. On account of this we have commenced to use the above described cassette, and with good results.

B. Radiological examination of operatively exposed uterus

As an ultimum refugium in the diagnosis of pregnancy the radiological examination of the exposed uterus has for certain cases now been adopted at the Gynecological Dept. Lund (Head Prof. ALF SJÖVALL). As the mobility of the embryo in the egg is considerable and as the embryonal skeleton is of low calcic content in the early stages, shortly exposed and sharply defined radiograms are of paramount importance. Experience has shown that it is impossible to use films without intensifying screens for this type of examination, and the ordinary cassette was inconvenient because its introduction was too difficult. For these reasons the author now suggests the new flexible type of cassette for this purpose. A detailed report of the use of such a cassette in diagnosing pregnancy will be published by OLLE OLSSON and SVEN SJÖSTEDT in Acta obstetr. et gynecol. scand.

SUMMARY

For the radiological examination of operatively exposed organs the author suggests the use of a rubber cassette of the type used in industry for the roentgen inspection of material. Flexible intensifying screens available in standard sizes are used. An easily sterilizable, flexible cassette with intensifying screens is thus provided.

ZUSAMMENFASSUNG

Zur Röntgenuntersuchung von operativ freigelegten Organen schlägt Verf. den Gebrauch einer Gummikassette vor, von dem in der Industrie zur Röntgenuntersuchung von Material verwendeten Typus. Es werden biegsame Verstärkerfolien verwendet, die in Standardgrössen zu haben sind. Hierdurch erhält man eine leicht sterilisierbare, biegsame Kassette mit Verstärkerfolien.

RÉSUMÉ

Pour l'examen radiologique d'organes mis à nu au cours des opérations l'auteur suggère l'emploi d'un châssis en caoutchouc du type utilisé dans l'industrie pour le contrôle des matériaux par les Rayons Roentgen. Il se sert d'écrans renforçateurs flexibles, disponibles dans les dimensions courantes. Ainsi l'on se procure un châssis aisément stérilisable, flexible et pourvu d'écrans renforçateurs.

REFERENCES

Åkerlund: Acta chir. scand. 74, 1937, p. 553.
Astraldi et Uriburn: Ref. Zbl. f. d. ges. Rad. 24, 1937, p. 518.
Beer: J. Urol. 25, 1931, p. 159.
Benjamin: J. Urol. 25, 1931, p. 165.
François: Proc.-Verb. L'Ass. Fr. d'Urol. Paris 1932, p. 616.
Heinèke: Münch. Med. Wschr. 54, 1907, p. 1753.
Heusser: Schweiz. Med. Wschr. II, 1937, p. 630.
Jaches ref. Benjamin.
Kneise u. Schober: Die Röntgenuntersuchung der Harnorgane. Leipzig 1941.
May: Z. Ur. 36, 1942, p 89.
Oppenheimer: J. Urol. 43, 1940, p. 253.
Petrén: Acta chir. scand. 77, 1936, p. 338.
Pflaumer: Z. Ur. 29, 1935, p. 225.
Pflaumer u. Friedrich: Gang und Technik der Röntgenuntersuchung auf Harnsteine, Leipzig 1940.
Priestley: S. G. O. 67, 1938, p. 798.
Puhl: Zbl. Chir. 1936, p. 1035.
Puigvert Gorro: Z. ur. Chir. 47, 1943, p. 32.
Quinby: Boston Med. a. Surg. J. 191, 1924, p. 194.
Sutherland: J. Urol. 33, 1935, p. 1.
Uebelhör: Z. ur. Chir. 41, 1936, p. 275.

FROM THE ORTHOPEDIC CLINIC OF THE CAROLINE INSTITUTE, STOCKHOLM, SWEDEN
(CHIEF: PROFESSOR STEN FRIBERG)

OBSERVATIONS ON THE GROWTH OF THE VERTEBRAL BODY IN SCHEUERMANN'S DISEASE[1]

by

Folke Knutsson

With reference to the increment of growth of the long bones we have exact knowledge owing to investigations carried out. Thus, by means of metal indicators various points of the growing bone have been marked and the increment of growth has been studied by registering the distance between these points. The rate of growth in the different epiphyses has thereby been made clear.

We have no correspondent knowledge of the increment of growth of the vertebral body. The embryonal development of a vertebral body is well known but the subsequent growth during childhood and adolescence of a fully developed vertebral body up to the termination of growth has not been scientifically investigated, as far as is known by the author.

It is known that growth of height takes place in the zone of ossification between the vertebral body and the cartilage plate and thus from two different directions but it is not known whether or not the increment of growth from the upper and the lower surfaces is uniform.

It is not either fully known how the growth of breadth and depth take place. Does this occur uniformly concentric to the center of the vertebral body or is the appositional growth unequal?

Experimental investigations that might lead to a complete understanding of the increment of growth of the vertebral body are lacking. It is, however, feasible to draw certain conclusions of the course of growth by studying the development of the vertebral body in cases of Scheuermann's disease. There is in this malady a disturbance of the zone of growth of an etiologically obscure nature. This disturbance of growth

[1] Also termed: Adolescent kyphose, Cyphose Juvénile douloureuse, Epiphysite vertébrale, Osteochondritis vertebralis.

Submitted for publication, April 27, 1948.

may involve the entire surface of the vertebral body or only a section thereof. As a consequence of this there occurs a general or more defined retardation of growth. Accordingly, this disease with the adequacy of an experiment causes a change in the rate of growth which in certain cases may be radiologically followed.

Horizontal growth

It has been feasible to study the horizontal growth in Scheuermann's disease on profile pictures of the spinal column. In appropriate cases it has hereby been possible to use a change in the surface of the vertebral body caused by an intracancellous disc prolapse as a fixed point in the investigations done at different ages.

These cases (fig. I—V) reveal that the horizontal growth of the vertebral body does not take place concentrically from the center of the vertebral body to the same extent in all directions. The transversal increment of growth has not been studied. With reference to the sagittal growth the investigation has shown that this exclusively takes place in the anterior direction. It is thus evident that in cases fig. I—III the appositional growth takes place from the anterior surface of the vertebral body. The cases fig. IV—V show that there has not occurred any demonstrable appositional increment of growth from the posterior surface of the vertebral body.

This condition of growth may be considered physiological, as there is no particular reason to assume that this type of growth only takes place in the presence of Scheuermann's disease. Thus, the vertebral bodies in fig. I, IV and V have an entirely normal geometrical shape.

It should, however, in this connection be pointed out that there exists a phenomenon of growth characteristic for Scheuermann's disease. The Scheuermann vertebra frequently has a greater sagittal depth than the adjoining normal vertebra (fig. II, III, VI, VII and VIII). It may be of practical importance to be aware of this factor. In vertebral fracture with compression trauma the vertebral body may namely become deformed to a general wedge-shaped compression, but it does hereby not attain an increased sagittal depth, unless there has occurred a frontal fracture through the vertebral body with diastasis. In the event of a differential diagnosis between a wedge-shaped or low vertebral body with an intact rectangular shape following Scheuermann's disease on the one hand, as against a deformation of the vertebral body following a fracture, on the other hand, it may thus be of importance to know that Scheuermann's disease commonly leads to an increased sagittal dimension of the vertebral body.

Fig. I 2460/43. Girl, born 1929. Vertebral body L. II. The intracancellous disc prolapse observed adjoining the anterior limbus edge 15. 4. 1943 remains as a hollow defect at examination 1. 12. 1943 and 8. 1. 1947. The vertebral body has undergone general growth. The distance between the disc prolapse and the posterior edge of the vertebral body is constant. It is thus shown that the sagittal growth of the vertebral body takes place in the anterior direction alone.

Fig. II 30033. Boy, born 1917. Vertebral body Th. X. The intracancellous disc prolapse surrounding the anterior limbus nucleus observed 2. 1. 1934 remains on 9. 6. 1936 as a hollow defect. The distance between the disc prolapse and the posterior edge of the vertebral body is constant. The sagittal growth of the vertebral body has thus taken place in the anterior direction.

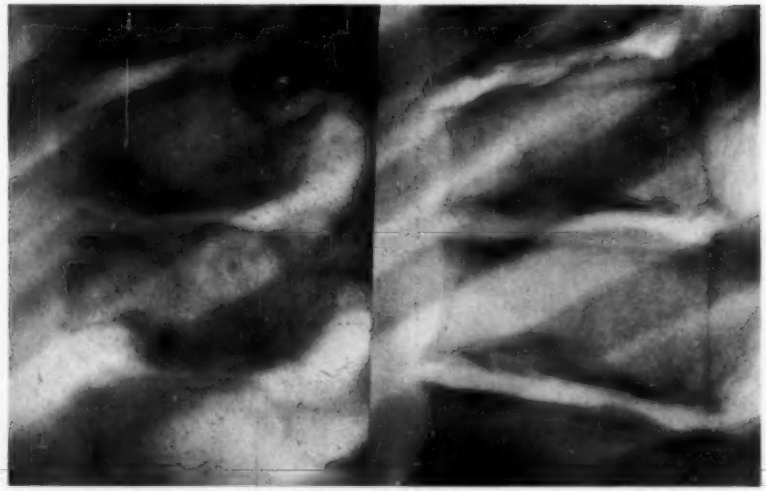


Fig. III 2400/9. Girl, born 1920. Vertebral bodies Th. VII and Th. VIII. The intracancellous disc prolapse at the anterior limbus edge observed 10. 3. 1932 remains as a hollow defect 7. 4. 1936. The distance from the disc prolapse to the posterior edge of the vertebral body is constant. The sagittal growth of the vertebral body has thus taken place in the anterior direction.

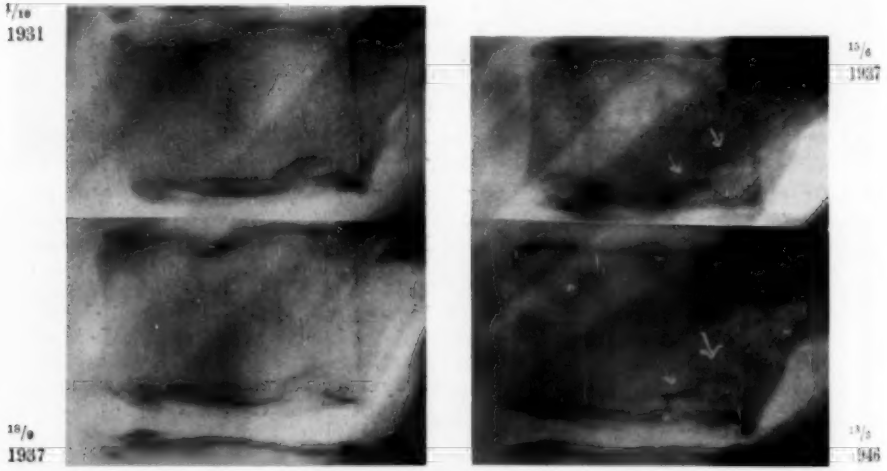


Fig. IV 2799/36. Boy, born 1922. Vertebral body Th. IX. The disc prolapse sited in the posterior section of the inferior surface has an unchanged position in relationship to the posterior edge of the vertebral body at examination 1. 10. 1936 and 18. 9. 1937. The vertebral body has grown in the sagittal direction and this growth has thus taken place anteriorly.

Fig. V 2291/36. Girl. born 1923. Vertebral body Th. IX. The disc prolapse sited in the posterior section of the inferior surface has an unchanged position in relationship to the posterior edge of the vertebral body. At examinations 15. 6. 1937 and 13. 3. 1946. The vertebral body has grown in the sagittal direction and this increment of growth has thus taken place anteriorly.

Fig. 6.

Fig. 7.

Fig. VI 158/36. Scheurmann's disease. Girl, aged 18. Vertebral bodies Th. VIII and Th. IX show a typical wedge-shape. Vertebral body Th. X, on the other hand, has an intact rectangular shape but is somewhat lower than normal. Th. VIII, IX and X all have an augmented sagittal depth.

Fig. VII 3811/44. Male, aged 21. Final stage of Scheuermann's disease. The vertebral bodies Th. VII and VIII are slightly wedge-shaped but Th. IX has an intact rectangular shape, although it is rather lower than the normal. All three vertebral bodies have an augmented sagittal depth.

Fig. VIII 6269/47. Male, aged 25. Final stage of Scheuermann's disease. The vertebral bodies Th. VII—VIII, and IX are wedge-shaped and all have an augmented sagittal depth.

Vertical growth

The disturbance in the zone of growth in Scheuermann's disease may involve a retardation of the rate of growth and the vertebral body may hereby become lower than the adjoining vertebral bodies.

In those particular cases in which the disturbance preponderantly involves the anterior sections of the zone of growth the typical *sagittal wedge-shape* arises. These wedgeshaped vertebrae that appear so distinctly on lateral roentgenograms of the thoracic spine are recognized as a characteristic deformity in Scheuermann's disease (fig. II, III, VI, VII and VIII).

In certain cases there is demonstrable a wedge-shaped deformation of the vertebral body laterally. In the same way as the sagittal wedgeshape leads to kyphosis, this *frontal wedge-shape* gives rise to a scoliostic curvature (fig. IX).

There is, however, very commonly found a vertebral body with an intact rectangular form but which is lower than the adjoining vertebral bodies. Peculiarly enough this deformity of the vertebral body so characteristic and frequent in Scheuermann's disease has not been noted in the literature, the wedge-shape alone having been pointed out. *This low vertebral body with an intact rectangular shape* probably is caused by a disturbance of growth uniformly distributed over the entire cross-section of the vertebral body (fig. VI, VII and VIII).

In summing up it may thus be said that the disturbance of growth which may arise in Scheuermann's disease either involves the entire cross-

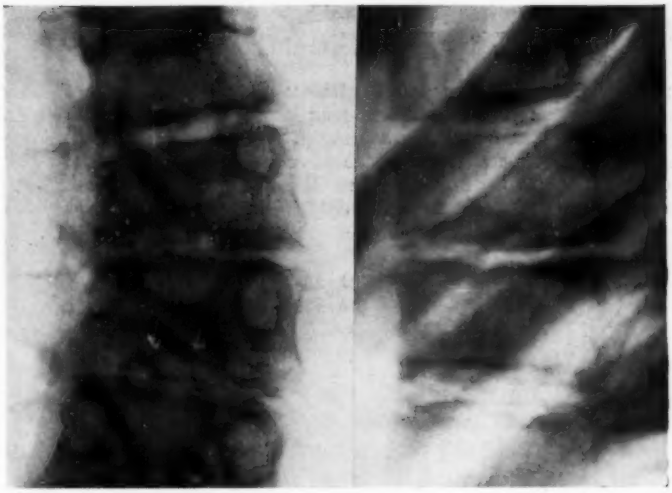


Fig. IX 1669/48. Girl, aged 13. Vertebral bodies Th. VIII and IX. These vertebral bodies show changes characteristic of Scheuermann's disease with irregularities of the surfaces of the vertebral bodies. These changes are limited to the one side and have hereby caused a disturbance of growth leading to a frontal wedge shape. Owing to this wedge shape of these both vertebral bodies there has arisen a scoliosis.

section of the vertebral body, this leading to its becoming lower than normal although with an intact rectangular shape, or, that it involves a limited section of the growth surface, whereby the vertebral body attains a wedge-like shape in the sagittal or the frontal plane.

SUMMARY

Scheuermann's disease may cause a disturbance of the *vertical growth* of the vertebral body which leads to a sagittal or frontal wedge-shape, or to the occurrence of a vertebral body lower than normal, although with an intact rectangular shape. It has with reference to the *horizontal growth* been demonstrated that this takes place by means of an appositional growth from the anterior surface of the vertebral body.

ZUSAMMENFASSUNG

Die Scheuermann'sche Krankheit kann eine Störung des *vertikalen Wachstums* des Wirbelkörpers hervorrufen, was eine sagittale oder frontale Keilform erzeugt, oder auch die Entstehung eines Wirbelkörpers von etwas unternormaler Höhe, aber mit erhaltener rektangulärer Form. Was das *horizontale Wachstum* anbelangt, so ist nachgewiesen worden, dass dieses durch appositionellen Zuwachs an der Vorderfläche des Wirbelkörpers stattfindet.

RÉSUMÉ

La maladie de Scheuermann peut entraîner un trouble dans la croissance en direction verticale du corps vertébral, ce qui rend la vertébre cunéiforme soit dans le plan sagittal, soit dans le plan frontal, ou encore fait qu'elle reste moins haute que normalement, tout en gardant ses contours rectangulaires.

En ce qui concerne l'accroissement en direction horizontale, on a démontré qu'il s'effectue par des appositions sur la face antérieure du corps vertébral.

AUS DEM EÖTVÖS LÓRÁND RADIUM- UND RÖNTGEN INSTITUTE, BUDAPEST, UNGARN

RÖNTGENSYMPTOME DER SPEISERÖHREN- UND MAGENVERLETZUNGEN DURCH ÄTZENDE GIFTE[1]

von

Dr *Iván Rodé*

Die Vergiftungen durch ätzende Mineralsäuren und -laugen sind früher in Ungarn ziemlich oft vorgekommen, weil die ätzenden Stoffe für Haushaltungszwecke für jedermann zugänglich waren. Auf wiederholten Drängen des Aerztestandes haben jedoch die in Jahren 1925 und 1928 gebrachten behördlichen Vorschriften den Verkauf ätzender Stoffe ausschliesslich auf gewerblichen Gebrauch beschränkt und so ist es gelungen, den grössten Teil dieser schweren Unfälle unmöglich zu machen.

Dieser Erfolg war auch vom Gesichtspunkt der Volksgesundheit aus sehr wichtig, weil bisher ein sehr grosser Teil der Pfleglinge der Kinderabteilungen und verschiedener anderer Abteilungen eben von diesen Opfern der ätzenden Gifte gestellt wurden. Wenn wir noch bemerken, dass nach der Statistik BALÁZS's die Mortalität bei Laugevergiftungen in allgemeinen 20.4 %, bei Säurevergiftungen aber 26.4 % beträgt, wird die ernste Bedeutung der ätzenden Gifte klar.

Überraschend ist jedoch, dass in Beziehung zu den dieses Problem behandelnden Arbeiten auf dem Gebiet der internen Medizin, Laryngologie, u. s. w. so wenig Veröffentlichungen vorliegen, die die Röntgensymptome der Vergiftungen ätzender Gifte darstellen.[2] Die Lückenhaftigkeit der ausländischen Literatur ist unser Meinung nach dadurch verständlich, da im Auslande diese Vergiftungen durch ätzende Stoffe sehr selten vorkamen. Aus diesem Grunde könnten die entsprechenden Daten nicht zur Verfügung stehen. Diese bisherige Lückenhaftigkeit der röntgenologischen Literatur auszufüllen ist das Ziel der beiliegenden Arbeit.

Bei den ätzenden Vergiftungen spielt die Röntgenuntersuchung eine ziemlich grosse Rolle. Das Entdecken der Speiseröhren- und Magenverletzungen, ihre Lokalisierung, die Überwachung der mit der Besserung oder Verschlechterung einhergehenden Veränderungen, die Entscheidung

[1] Bei der Red. am 15. 6. 1947 eingegangen.

[2] BOCK und HIN, GALDAU und POPP, TESTA.

über den Zeitpunkt und die Art und Weise eines etwaigen chirurgischen Eingriffs, u. s. w. sind alle sehr ernste und unentbehrliche röntgenologische Aufgaben. Gleichzeitig bedeutet die Untersuchung der Veränderungen anderer Organe (Lunge, Brustfell, Schlund u. s. w.) ein ausgedehntes Arbeitsfeld.

Neben der Unterstützung anderer Untersuchungen und deren Ergänzung, hat die Röntgenuntersuchung auch eine anderweitige Aufgabe: die einer selbständigen diagnostischen Tätigkeit, indem sie entscheidet, ob eine gewisse chronische Speiseröhren- oder Magenveränderung geschwürigen, geschwulstigen oder eben verätzenden Ursprungs ist. In Anbetracht dessen, dass die Kranken, die das Gift aus selbstmörderischer Absicht eingenommen haben, diesen Umstand oft aus Schamgefühl verheimlichen oder einfach anzugeben vergessen, ist die Feststellung der wirklichen Natur solcher chronischer Veränderungen eine sehr schwere, ja manchmal unlösbare, röntgenologische Aufgabe.

Endlich dürfen wir auch nicht ausser Acht lassen, dass wir bei den experimentell hervorgerufenen ätzenden Vergiftungen über die funktionellen Veränderungen nur durch die Röntgenuntersuchung einen Aufschluss erhalten können.

Es ist also festzustellen, dass in Zusammenhang mit den Vergiftungen durch ätzende Mittel die Röntgenuntersuchung eine sehr grosse Rolle spielt u. zw. in Allgemeinem auf drei Gebieten: 1) die Unterstützung und Ergänzung anderer Untersuchungen, 2) die selbständige diagnostische Tätigkeit, 3) die Klärung der funktionellen Veränderungen bei Versuchen. Die Grundlage zur Untersuchung der Röntgensymptomatologie der nach ätzenden Giften entstandenen Speiseröhre- und Magenverletzungen haben 79 Fälle von Laugevergiftungen, 29 von Säurevergiftungen und 3 Fälle von mit anderen ätzenden Mitteln Vergifteten gegeben. Von den mit Lauge Vergifteten waren 78 Frauen und 1 Mann. Das durchschnittliche Alter der Frauen war 22 Jahr; die Jüngste war 14, die älteste 59 Jahre, der Mann 25 Jahre alt.

Das eingenommene Gift war bei allen mit Lauge Vergifteten: NaOH. Die mit Säuren vergifteten waren ausnahmlos Frauen. Das durchschnittliche Alter betrug 24 Jahre; die Jüngste war 17, die älteste 47 Jahre alt. Das eingenommene Gift war in den meisten Fällen Salzsäure (24), sonst Schwefelsäure (2), Oxalsäure (2) und Ameisensäure (1). Unter den anderen ätzenden Giften sind Kaliumpermanganat (1), Chlorzink (1) und Formalin (1) vorgekommen; diese behandeln wir bei den mit Säuren Vergifteten, da sie ebenfalls eine Koagulationsnekrose verursachen.

Wir haben nach Einnahme von Lauge in 18 Fällen, nach Säureeinnahme in 9 Fällen weder an der Speiseröhre noch im Magen irgendeine pathologische Veränderung gefunden. Bei den übrigen Fällen haben sich entweder an der Speiseröhre oder am Magen oder an beiden Organen

mehr oder weniger ausgeschprochene Veränderungen gezeigt. Die Veränderungen haben sich in leichteren Fällen nur als Spasmen, in schwereren Fällen als Vernarbungen gezeigt. Der Spasmus ist in machen Fällen spurlos verschwunden, in anderen Fällen jedoch ist danach eine Vernarbung entstanden. Vor der Beschreibung der verschiedengradigen Verletzungen halten wir es jedoch für notwendig, bezüglich der ätzenden Vergiftungen, einige allgemeingültige Bemerkungen anzuschliessen.

Die Schwere der in der Speiseröhre und im Magen entstandenen Verletzungen hängt einerseits von den Eigenschaften des Ätzmittels — hauptsächlich von seiner Konzentration und Menge — andererseits von den in dem Verdauungskanal herrschenden Verhältnissen (Füllung, Schleimbelag u. s. w.) ab. Unter Berücksichtigung dieser Gesichtspunkte kann man alle Verletzungsmöglichkeiten erklären. Da wir die Wiederholungen vermeiden wollen, erwähnen wir über die diesbezüglichen Daten nur soviel, wie zum Deuten der Röntgensymptomen unbedingt notwendig ist.

Es ist eine allgemeine Beobachtung, dass die Verletzungen der Speiseröhre besonders bei Säurevergiftungen seltener und weniger schwer sind, als die des Magens. Die Erklärung dieser Tatsache ist wahrscheinlich darin zu finden, dass das Schlucken ein sehr schneller Vorgang ist. Bei der Weiterbeförderung des Geschluckten spielt die Gravitation, das heisst das Gewicht des Geschluckten und die Muskulatur eine Rolle. Die Schwerkraft spielt jedoch eine sehr untergeordnete Rolle, da unter deren Wirkung das Schlucken nur ein sehr langsamer Vorgang wäre. Die Schnelligkeit des Schluckvorgangs ist eben dadurch erklärt, dass sie das Ergebnis einer aktiven Muskeltätigkeit ist. Die Schlundschnürmuskeln und die Muskeln des oberen Teiles der Speiseröhre sind quergestreift, nur an dem unteren Segment der Speiseröhre finden wir glatte Muskeln. Es ist bekannt, dass die quergestreifte Muskulatur eine Fähigkeit zu sehr schneller Kontraktion hat. Infolgedessen spritzen die Schlundschnürmuskeln in der ersten Phase des Schluckens sozusagen den Geschluckten in den oberen Teil der Speiseröhre hinein, von wo die ebenfalls quergestreifte Muskulatur ihn schnell gegen die Cardia weiterbefördert. Die Bewegungsgeschwindigkeit des Bissens lässst nur in dem unteren Teil der Speiseröhre einigermassen nach, weil die Kontraktion der hier befindlichen glatten Muskulatur träger ist. Auch das Warten auf das Öffnen der Cardia bedeutet eine Verspätung und eigentlich ist dies der einzige Umstand, durch den der Schluckakt bedeutend verlängert wird. Zeitlicher verhält sich das annähernd so, dass der Geschluckte ungefähr in einer Sekunde bis zum Cardia, dann nach 5—6 Sekunden Warten in den Magen gelangt. Der ganze Verlauf des Schluckens dauert also nur 6—7 Sekunden. Diese aussergewöhnlich kurze Zeit, sowie die eigentümliche Verteilung der Zeitspannen im Verhältnis zu den verschiedenen Teilen der Speiseröhre verursachen, dass die Verlet-

zungen im Allgemeinen seltener und weniger schwer sind, besonders in den oberen Teile der Speiseröhre, weil dem Gift nicht genügend Zeit zur Verfügung steht, eine tiefere Wirkung auszuüben. Auffallend ist jedoch, dass die oben angeführte Überlegung sich vorwiegend auf die Säuren bezieht, die wirklich wenigere Speiseröhreverletzungen verursachen, als die Laugen.

Dagegen sind nach dem Einnehmen von Ätzlauge die Speiseröhrenverletzungen ziemlich häufig und schwer. Die Frage ist, welche die Ursache dieser Abweichung ist. Die Wirkung der ätzenden Stoffe ist unabhängig von ihrer Natur ziemlich gleich. Beide verursachen, als ätzende Mittel, abhängig von ihrer Konzentration und Menge, eine ätzende Wirkung, die bei einem schwereren Grad eine Gewebenekrose hervorbringt. Wir müssen aber auf den Umstand hinweisen, dass auf die Einwirkung der Säure eine trockene Gerinnungs-Nekrose (coagulatio), auf die Einwirkung einer Lauge hingegen eine wässerige Auflösungs-Nekrose (colliquatio) folgt. Der durch die Säure gebildete Flüssigkeitsärmere dichte Schorf hemmt die weitere ätzende Wirkung; die durch die Einwirkung einer Lauge nekrotisierten, wässerigen lockeren Gewebe befördern hingegen das weiter in die Tiefe Dringen des ätzenden Stoffes. Den Unterschied zwischen den beiden Wirkungen charakterisiert BALÁZS sehr treffend so, dass sich die Gewebe, gegenüber den Säuren, so wie Schreibpapier, gegenüber den Laugen jedoch wie Löschpapier verhalten. Dieser wichtige Wirkungsunterschied macht es verständlich, dass so wie überall, auch in der Speiseröhre, die Laugen öfters und schwerere Verletzungen hervorrufen als die Säuren.

Die oben besprochenen Verhältnisse finden auch in unserem Material eine Bestätigung. Bei Säurevergiftungen finden wir nur bei 3—5 %, bei Laugevergiftungen hingegen bei 32 % Speiseröhren-Verengerungen.

Die Stellen der Verletzungen der Speiseröhre sind in Allgemeinen die auch physiologisch schon engere Stellen, so besonders der Anfangsteil, die Höhe der Luftröhren-Verzweigung, die Cardia. An anderen Stellen erstehende Verletzungen erklärt MEHNERT damit, dass die Speiseröhre auch an anderen Stellen physiologische Verengungen hat, z. B. bei der Kreuzung mit der linken Bronchie und mit der Aorta, die bei normalen Verhältnissen kaum bemerkbar sind, aber durch nach verätzender Wirkung entstandenen Gewebsquellungen ausgesprochener werden. Weitere Aufklärungen vermitteln die Tierversuche TESTA's. TESTA hat Hunden durch Sonden eine 15 %-ige Lauge eingegeben und dabei festgestellt, dass die nacheinander sich folgenden Schlücke infolge des Cardiakrampfes sich säulenartig aneinanderschichten. Es ist klar, dass Ätzungen abhängig von der Höhe der Säule auch an Stellen zwischen den physiologischen Engen vorkommen können.

Wir haben bereits erwähnt, dass die Verletzung der Speiseröhre in

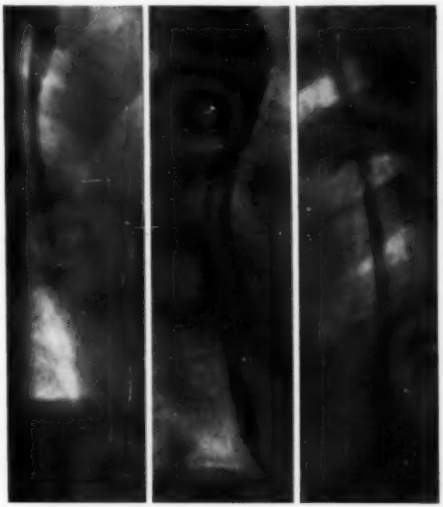


Bild 1. Bild 2. Bild 3.

Bild 1. Lauge-Vergiftung: 3 Monate nach der Vergiftung: an der Speiseröhre ist durch eine Suspension kein Spasmus nachwiesbar.

Bild 2. Derselbe Fall: an dem oberen Teil des thorakalen Abschnitts der Speiseröhre sind mit einem Brei 2 ringförmige spastische Verengerungen nachweisbar.

Bild 3. Lauge-Vergiftung. $2^1/_2$ Jahre nach der Vergiftung. Das Bild der »inaktiven Oesophagus» Säulenartige, walzenförmige Speiseröhre, die in jedem Durchmesser gleich ist und die das Bild einer sich im Tonus befindlichen Speiseröhre nicht zeigt.

leichteren Fällen in Form eines Spasmus auftritt. Nach eine Säurevergiftung ist ein solcher Fall nicht zur Untersuchung gelangt. Unsere Beobachtungen beziehen sich auf mit Lauge Vergifteten, bei den wir in 11 Fällen einen Speiseröhren-Spasmus feststellen konnten, und zwar in 7 Fällen im thorakalen Teil, in 4 Fällen im kardialen Abschnitt. Vor dem Durchleuchtungsschirm sieht man gewöhnlich, dass der erste Schluck unbehindert hinuntergeht, nach dem zweiten—dritten Schluck hingegen ein Spasmus entsteht, den ohne Zweifel die Berührung des Schluckens mit der geätzten Schleimhaut reflektorisch hervorruft. Es ist für den Spasmus der Speiseröhre charakteristisch, dass er nach der Gabe krampflösende Mittel aufhört und so seine funktionelle Natur leicht erkennbar ist.

Wir müssen hier bemerken, dass die Feststellung des Spasmus nicht immer so einfach gelingt. Es kann nähmlich vorkommen, dass dieser sich bei einer dünnen Suspension nicht meldet, sondern nur bei dem Anwenden eines dicken Breies (stärkerer Reiz). Diese kann umso leichter vorkommen, weil es eben bei einem Verdacht auf eine Speiseröhrenverletzung nicht üblich und auch nicht zu empfehlen ist, einen dicken Brei schlucken zu lassen. Unsererseits haben wir einmal diese Schwierigkeit angetroffen (Bild 1). Bei der ersten Untersuchung hat die Suspension ungehindert die ganze Speiseröhre durchflossen: wir haben keinen Spasmus gesehen. Bei der mit Brei wiederholten Untersuchung hat sich jedoch herausgestellt, dass in der Höhe des Schlüsselbeines und zwei Fingerbreit unter

ihm, je eine ringartige, spastische Verengerung vorhanden war (Bild 2). Im Zusammenhang mit dem Speiseröhren-Spasmus wollen wir die Aufmerksamkeit darauf lenken, dass diesen nicht nur lokale Ursachen, sondern auch in der Nachbarschaft sich abspielende Prozesse aufrechterhalten können. In der Literatur sind mehrere diesbezügliche Veröffentlichungen bekannt. Es haben ihn beobachtet: ASSMANN bei verkalkten Drüsen, PALUGYAY bei tiefliegenden Speiseröhrendivertikeln, andere in den Fällen von Venenerweiterungen und von peptischen Geschwüren. Eben deshalb ist im gegebenen Fall oft schwer zu entscheiden, ob wir den vorliegenden Krampf der Wirkung des ätzenden Stoffen oder anderen Ursachen zuschreiben sollen. Wir haben bei einem unserer Fälle am unteren Abschnitt der Speiseröhre eine spastische Verengerung festgestellt. Wir hätten den Spasmus ohne weiteres mit der Wirkung des ätzenden Giftes im Zusammenhang gebracht, aber als Nebenbefund haben wir auch einen tiefliegenden, erbsengrosser Divertikel gefunden. In der Kentniss der obenerwähnten Beobachtungen ist zweifelhaft geworden, ob der Spasmus von dem ätzenden Gift oder von dem Divertikel verursacht wurde. Die Frage hätten wir dadurch entscheiden können, dass wir die Untersuchung nach der angenommenen Regeneration der Ätzung wiederholten, wenn der Spasmus auch dann noch bestehen geblieben wäre, hätte ihn wahrscheinlich der Divertikel ausgelöst. Leider, haben wir dazu keine Gelegenheit gehabt, weil die Kranke sich zur weiteren Untersuchungen nicht gemeldet hat.

Das Röntgenbild der narbigen Speiseröhrenverengerungen ist sehr charakteristisch. Man sieht in entsprechender Höhe der Speiseröhre eine ring- oder röhrenförmige, auf längerem oder kürzerem Abschnitt sich ausdehnende, scharfrändige Verengerung, und oberhalb dieser die oralen Teile der Speiseröhre sich ausweiten. Zu ihrer Charakterisierung erwähnen wir zwei Fälle. Die eine hat vor 35 Jahren eine Laugevergiftung durchgemacht.

Im oberen Drittel des thorakalen Teiles der Speiseröhre befand sich in der Höhe des Schlüsselbeines eine ringartige fadendünne Verengerung oberhalb dem der orale Teil der Speiseröhre sich mässig erweitert. Die zweite Kranke hat 5 Monate vor der Untersuchung Lauge geschluckt: hier hat sich am unteren Drittel des thorakalen Teiles der Speiseröhre eine bis zur Cardia sich ausbreitende narbige Verengerung entwickelt durch die das Kontrastmittel nur in fadendünnen Strahl durchtreten konnte. Die Erweiterung der oberhalb liegenden Teile war hier schon ausgesprochener. Wir müssen daran denken, dass wir im Zusammenhang mit der Untersuchung der im unteren Drittel der Speiseröhre entwickelten Verengungen, die Länge dieser unter Ausschluss jeden Zweifels nur so feststellen können, wenn wir die Kranken nicht nur in aufrechter, sondern auch in liegender Stellung untersucht haben. Über die Verengerungen

gelangt nähmlich nur wenig Kontrastmittel in die tieferliegenden Teile der Speiseröhre und dies erweckt den Eindruck, als ob die Verengerung sich bis zur Cardia ausdehnen wurde. Von dieser Irrtum bewahrt uns die Untersuchung in der Rückenlage.

Bei den Nachweis der narbigen Verengungen kann die richtige Auswahl der Dicke des Kontrastmittels ebenso sich als notwendig erweisen, wie im Falle eines Spasmus. Bei einer vor 4 Monaten mit Lauge vergifteten Kranken haben wir beim Schluckenlassen einer dünnen Suspension eine im unteren Drittel der Speiseröhre sich bis zur Cardia ausbreitende Verengerung gesehen, oberhalb derer die Speiseröhre sich ausgesprochen ausgeweitet hatte. Beim Schluckenlassen eines dicken Breies konnten wir auch auf der Grenze zwischen mittleren und oberen Drittel eine Verengerung, zusammen mit einer oberhalb derer sich befindenden Ausweitung, nachweisen.

Die Differentialdiagnostik der narbigen Verengungen der Speiseröhre verursacht keine Sorgen. In erster Reihe kommt die Differenzierung von den Spasmen in Frage. Die gelingt aus dem Grund ohneweiteres, weil sie auch nach dem Geben krampflösender Mittel bestehen bleiben, also einen ständigen Charakter haben. Manchmal müssen wir gegenüber karzinomatösen Verengerungen differenzieren: die letzteren haben jedoch zerfressene Ränder und die infolgedessen auftretenden Erweiterungen erreichen nie einen grossen Grad, da der Kranke schon vorher durch Auszehrung zugrunde geht. Natürlich bedeutet in jeden zweifelhaften Fall die Anamnese einen entscheidend wichtigen Wegweiser.

Im Zusammenhang mit den Verletzungen der Speiseröhre, erwähnen wir die Notwendigkeit einer Untersuchung auch des hinteren Mediastinums. Nach den Beobachtungen UDVARDYS, ist — ausgenommen die ganz leichten Fälle — das hintere Mediastinum immer verdeckt. Dieses Symptom entsteht infolge der Entzündung der Speiseröhre und wird durch das entzündliche Exsudatum der benachbarten Organe verursacht. Dies ist natürlich nicht charakteristisch für die ätzenden Vergiftungen, da dies auch bei andersartigen Prozessen in der Speiseröhre auftreten kann (verschluckte steckengebliebene Fremdkörper, im Zerfall befindliche Geschwülste usw.). Seine Bedeutung besteht darin, dass es prognostisch auswertbar ist: eine Verminderung der Verdecktheit des Mediastinums bedeutet auch eine Verminderung der Entzündung der Speiseröhre und umgekehrt.

Zum Schluss muss noch eine besondere Form der Speiseröhre-Verletzung besprochen werden, welche nach unserem Wissen von anderen Beobachtern noch nicht besprochen wurde. Das Krankheitsbild haben wir in 3 Fällen sich nach Laugeverätzungen entwickeln sehen.

Klinisch bestanden die Symptome einer impermeabilen Speiseröhreverengerung: die Kranken konnten auch flüssige Speisen nicht schlucken.

Bei der Durchleuchtung haben wir festgestellt, dass das dünne Kontrastmittel nur in den obersten Teil der Speiseröhre gelangen konnte, dort jedoch stecken blieb und nicht weiter kam. Bei vorsichtigen Sondierungsversuchen hat sich zu unserer Überraschung herausgestellt, dass auch die Sonde mit dem grössten Durchmesser bis zur Cardia durchführbar war. Mit einem durch eine Sonde eingeführten dünnen Kontrastmittel konnte man die Speiseröhre bis zur Cardia ausfüllen. Danach hat sowohl die Sondierung als auch die Röntgenuntersuchung das Bestehen einer Verengerung ausgeschlossen. Es entstand die paradoxe Lage, dass bei vollkommener Schluckunfähigkeit ein mechanisches Hindernis nicht nachzuweisen war. In Anbetracht dessen, dass uns keine Sektionsmaterial zur Verfügung steht, sind wir bei der Erklärung des Krankheitsbildes nur auf Vermutung angewiesen. Wir müssen für wahrscheinlich halten, dass die Schluckunfähigkeit durch ein durch die Laugeverätzung hervorgerufene Verletzung der Muskulatur oder der Nerven verursacht wird, die auf direkten oder indirekten Wege die aktive Mitarbeit der Muskulatur in dem Schluckverlauf unmöglich macht. Wir nennen eben auf Grund dieser Überlegungen diesen aussergewöhnliche Krankheitsbild »inaktiver Oesophagus».

Zur Charakterisierung dieser Verletzung veröffentlichen wir nur eine Aufnahme, da sie keine besonderen röntgenologischen Eigentümlichkeiten zeigt (in den anderen zwei Fällen haben wir uns mit einer Durchleuchtung begnügt). Das durch die Sonde eingeführte Kontrastmittel zeigt eine säulenartige, walzenförmige Speiseröhre (Bild 3), die in allen ihren Durchmessern gleichmässig ist und die das bekannte Bild einer sich in normalem Tonus befindlichen Speiseröhre, nämlich einen mit der Spitze nach unten stehenden Kegel, nicht zeigt. Als ein Zeichen der Inaktivität der Muskulatur ist eine Peristaltik nicht zu beobachten. Es ist vielleicht überflüssig zu erwähnen, dass im Falle eines »inaktiven Oesophagus» eine Gastrostomie unbedingt durchzuführen war, ebenso wie bei einer echten impermeabilen Verengerung.

In der Einleitung wurde davon gesprochen, dass der Grad der Verletzungen im allgemeinen im Verhältniss zur Konzentration und zur Menge des ätzenden Mittels steht. Beim Übergang zu den Ätzungsverletzungen des Magens, müssen wir noch hinzufügen, dass im Magen auch andere Faktoren mitspielen. Hier hängt die Wirkung auch davon ab, ob der Magen beim Eindringen des Giftes leer oder voll und ob die Schleimhaut durch einen Schleimbelag geschützt war. Wenn der Magen leer ist und die Schleimhautfalten sich berührend aneinanderliegen, dann kann sich die Verletzung auf die ganze Innenwand des Magens ausdehnen; wenn er dagegen voll ist, dann übt das ätzende Gift seine stärkste Wirkung auf die kleine Kurvatur und auf den antralen Teil aus. Diese letztere Lokalisation der Verletzungen ist durch die normalen Verhältnisse zu e-

klären. Der bei normalen Verhältnissen in den Magen gelangende Bissen bewegt sich auf der sogenannten »Waldeyerischen Magenstrasse» weiter. Nach den Untersuchungen FORSSELLS umschliessen die Magenfalten infolge der Kontraktion des Muscularis mucosae den Bissen eng und schaffen sogenannte Digestions-Kammern, die einen vollkommenen Abdruck des Bissens darstellen. Die um die ätzende Lösung sich mit den Kanten berührenden Magenfalten bilden einen Kanal um die kleine Kurvatur und verlangsamen auf diese Weise ihre Weiterbewegung. Die Stelle der ersten Verätzung wird danach die kleine Kurvatur. Im weiteren Verlauf gelangt der ätzende Stoff in den antralen Teil und löst dort infolge seiner chemischen Wirkung — zu der sich noch der Schmerz gesellt — einen Pylorus-spasmus aus; der Pylorus also schliesst sich und das ätzende Gift sammelt sich im Antrum. Es ist klar, dass die nächstfolgende und schwerere Verletzung den Pylorus trifft. Dieser Spasmus kann sich mit der Zeit lösen, aber wenn die Ätzung sich sehr in die Tiefe verbreitet und auch den Auersbach- und Meissner-Plexus erreicht hat, dann kann als Folge eine Magenlähmung oder motorische Insuffizienz auftreten. Auf Grund dieser Überlegungen könnte eigentlich eine Verletzung des Pylorus nur mit einer gleichzeitigen, beziehungsweise vorangehenden Verletzung der kleinen Kurvatur entstehen. Es ist jedoch allgemein bekannt, dass bei ätzenden Vergiftungen oft eine isolierte Pylorus-Verletzung — unser Meinung nach wegen des verminderten Tonus des Magens — vorkommt. In den hypotonischen und atonischen Magen fällt nämlich sozusagen der Bissen und auch das Gift hinein und gelangt ohne Verzögerung bis zum Pylorus. Andererseits muss man auch das in Betracht ziehen, dass zwischen Laugen und Säuren ein bedeutender Unterschied in der Viscosität besteht. Die stark viscose Lauge haftet sich auf ihrem Wege überall an: es ist verständlich, dass sie in erster Reihe die Speiseröhre verätzt. Die weniger viscose Säure kann hingegen durch die Speiseröhre gehen und ätzt dann dort an stärksten, wo sie sich infolge der anatomischen Verhältnisse sammelt, also eben im pylorischen Teil. So wird schon ohne weiteres der Mechanismus der isolierten Verletzungen des Pylorus verständlich.

Die oben skizzierten Verhältnisse kann man auch durch Versuche bestätigen. Wir berufen uns wieder auf die Hundeversuche TESTA's. Nach diesen spielen sich die Veränderungen durch die Wirkung von in den Magen gelangten Giften in zwei Phasen ab. In der ersten Phase entsteht am Antrum ein Spasmus. Der Pylorus schliesst sich und die Peristaltik hört auf. In der zweiten Phase löst sich der Spasmus und es entsteht eine stürmische Peristaltik, sogar eine Antiperistaltik, die den Inhalt des Magens teilweise gegen die Cardia drückt, teilweise in das Duodenum. Auf diesen letzteren Moment kehren wir noch in dem Teil über die Verletzungen des Duodenums zurück.

Da die Stellen der stärksten Einwirkung regelmässig die kleine

Kurvatur und der Pylorus sind, hat dieser Umstand einige Autoren zu der vorschnellen Ansicht verleitet, dass der Fundus des Magens immer heil bleibt. Die Ursache wäre dafür die Schutzwirkung der Magenluftblase. Die durch Sektion bestätigten Fälle BALÁZS's beweisen jedoch etwas anderes. Es hat sich nämlich herausgestellt, dass in gewissen Fällen auf dem Fundus noch ausgesprochenere Verletzungen waren, als an der kleinen Kurvatur oder am Pylorus. BALÁZS erklärt das damit, dass die Stelle der Verletzung in Magen nicht nur von dessen Füllung, sondern auch von der Körperlage abhängt. Der Vergiftete bricht meist durch die heftigen Schmerzen zusammen, wältzt sich von einer Seite auf die andere, wirft sich in seinen Qualen herum und so kann das ätzende Gift abhängig von der Körperlage an jede Stelle des Magens, also auch an den Fundus, gelangen. Die hier entstandene Verletzung kann die vorher erwähnte Antiperistaltik noch mehr steigern, welche den ätzenden Stoff hinpresst. Zweifellos ist die Magenluftblase fähig eine Schutzwirkung auszuüben. Man darf jedoch nicht ausser Acht lassen, dass sie nicht immer den Fundus schützt. Die Magenluftblase nimmt nämlich infolge ihres spezifischen Gewichts ihre Stelle immer am höchsten Punkt des Magens ein, schützt also nur in stehender Haltung des Fundus, sonst jedwelchen Teil des Magens, wohin sie eben entsprechend der Körperlage gelangt ist. Die Verletzungen des Magens können abhängig von den schon erwähnten Faktoren also verschieden sein. Das pathologisch-anatomische Bild der Verletzungen ist allgemein bekannt. Damit wollen wir uns auch nicht des Breiteren beschäftigen und weisen nur auf die entsprechenden Beschreibungen hin.

Vom röntgenologischen Gesichtspunkt aus haben wir, auf Grund der gesehenen Bilder, die Veränderungen in drei Gruppen eingeteilt: 1. Schleimhaut-Veränderungen, 2. Spastische Erscheinugen, 3. Vernarbungen.

Diese Veränderungen können natürlich auch miteinander verbunden auftreten, da die Wirkung auf die verschiedenen Teilen des Magens nicht immer gleich ist. Bei oberflächlicher Einwirkung wird nur die Schleimhaut verletzt, eventuell zeigt sich auch ein Spasmus, bei der in die Tiefe dringender Einwirkung entstehen Vernarbungen. Die Folgen einer oberflächlichen Einwirkung bilden sich bald aus: diese sind also Frühveränderungen. Zur Entwicklung einer Vernarbung ist eine längere Zeit notwendig; diese gehören also zum Kreis der Spätveränderungen.

Bei Säure-Vergifteten hat sich die Schleimhautveränderung in 4 Fällen nur in einer Schwellung der Falten gezeigt, dem einfachen hypertrophischen Magenkatarrh ähnlich. Diesen einfachen Typ demonstrierte einer unserer Fälle, der am 15. Tage nach der Salzsäure-Vergiftung untersucht wurde. Die Falten waren stark geschwollen, gewunden und an der Fundus-Gegend war das Relief nicht zu sehen.

Bei 9 anderen unserer Fälle haben jedoch die Falten ein sehr eigentümliches und bezeichnendes Bild gezeigt. Die stark geschwollenen und breiten Falten, welche einen mehr oder weniger gewundenen Ablauf zeigten, haben mit dem schmalen, zwischen den Falten liegenden Furchen, unregelmässige, vieleckige Formationen gebildet, die in ihrer Gesammtheit eine an den Bienenwaben erinnernde Zeichnung gegeben haben. (Bild 4.) Diese charakteristische wabenartige Zeichnung hat sich manchmal auf die ganze innere Schleimhautoberfläche ausgedehnt, in anderen Fälle ist sie nur stellenweise, an dem oberen oder unteren Drittel des Magenkörpers, eventuell in der Gegend der grossen Kurvatur (Bild 5) sichtbar geworden und so hat sich die Zeichnung der einfach geschwollenen Falten mit der wabenartigen Zeichnung in mannigfaltigster Weise verwebt.

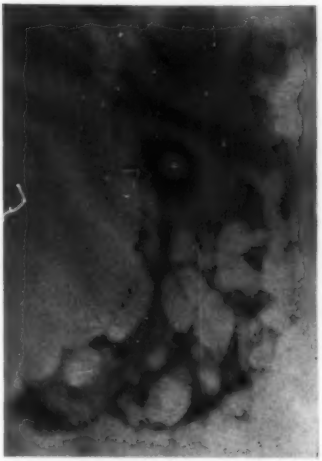


Bild 4. Salzsäure-Vergiftung. 16. Tage nach der Vergiftung: die stark geschwollenen und breiten Falten bilden mit den schmalen zwischen den Falten liegenden Furchen unregelmässige, vieleckige Formationen, die in ihrer Gesamtheit eine an Bienenwaben erinnernde Zeichnung geben.

Die wabige Zeichnung gehört zweifellos zu den Frühveränderungen des mit Säuren vergifteten Magens, den genauen Zeitpunkt ihrer Auftretens kennen wir jedoch nicht. Wir haben sie am frühesten am 6. Tage nach der Vergiftung nachgewiesen, was jedoch nur soviel bedeutet, dass ein frischerer Fall nicht zur Untersuchung gelangt ist. Die Veränderung selbst könnte schon gleich nach Einnahme des Giftes bestehen, sowie der einfache hypertrophische Magenkatarrh, den wir am 1. Tage nach der Vergiftung gesehen haben. Von der Zeitspanne, sowohl ihres Fortbestehens, als auch ihrer Regeneration, haben wir jedoch schon genauere Daten. Wir haben nämlich die Gelegenheit gehabt das Schicksal einer unserer Kranken von der Vergiftung bis zur Heilung kontrollieren können.

Die Kranke ist am 6. Tage nach Einnahme des Giftes (Salzsäure) zur Röntgenuntersuchung gelangt. Wir haben an der Schleimhaut eine sehr ausgedehnte wabige Zeichnung beobachtet, die auf der ganzen Innenoberfläche des Magens sich verbreitete. Am 15 Tage nach der Vergiftung war die wabige Zeichnung weniger ausgesprochen, aber noch behalten. Diese Veränderung ist erst am 60. Tage verschwunden, als wir am Magenrelief wieder die normal breite und normal angeordnete Zeichnung der Falten beobachtet haben. Nach unserer Beobachtungsreihe hat

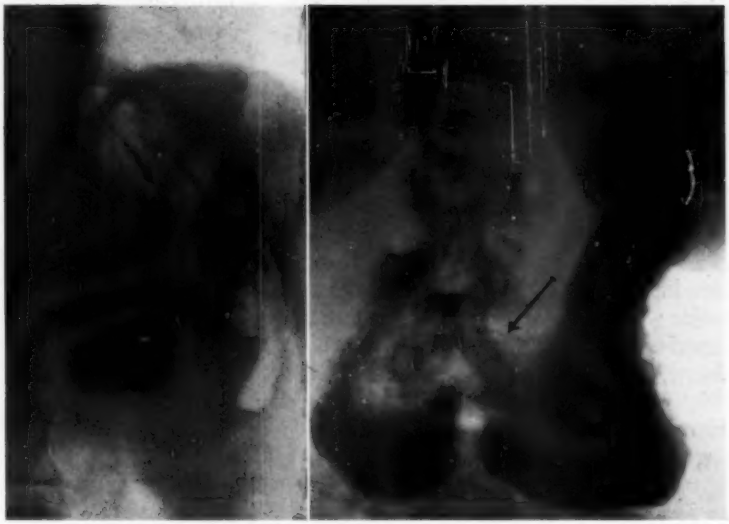


Bild 5. Bild 6.

Bild 5. Salzsäure-Vergiftung. 6. Tage nach der Vergiftung: wabige Zeichnung in der Gegend der grossen Kurvatur.

Bild 6. Salzsäure-Vergiftung. Antrumvernarbung. 9. Tage nach der Vergiftung: der antrale Abschnitt des Magens ist röhrenförmig verschmälert, das Kontrastmittel durchschiesst ihn, die Entleerung ist schnell.

also das Verschwinden der eigenartigen Zeichnung, d. h. die Regeneration der Schleimhaut, zwei Monate lang gedauert.

Die nähere Ursache der Veränderung ist nicht bekannt. Wir können nicht sagen, warum in dem einen Falle nur ein einfacher Magenkatarrh, in dem anderen eine wabenartige Zeichnung auftritt. Sicher ist jedoch dass sie nur bei Säure-Vergiftungen vorkommt. Die Erscheinung ist um so interessanter, als sie beweist, dass *zwischen Säure- und Laugewirkung ein qualitätiver Unterschied vorhanden ist.* Die Ursache ihres Auftretens ist, da wir sie auch bei anderen Säure-Vergiftungen gesehen haben, so z. B. nach Einnahme von Schwefelsäure, zweifellos die *sauere chemische Reaktion.*

Aus dem Umstand, dass diese in den Sektionsbefunden nicht erwähnt wird, können wir folgern, dass sie funktioneller Natur ist, eine nur bei Lebenden vorkommende Veränderung, also eigentlich ein Symptom, dessen Kenntnis wir ausschliesslich der Röntgenuntersuchung verdanken.

Im Anbetracht dessen, dass die wabenförmige Zeichnung chara-

teristisch ist und nur bei Säurevergiftungen vorkommt, ist sie differen-ial-diagnostisch verwertbar: wenn wir dieses Bild sehen, ist die Diagnose bestimmt die einer Säurevergiftung.

Zur Ergänzung erwähnen wir noch, dass wir bei unserer mit Ameisen-äure vergifteten Kranken nur eine starke Schwellung des Faltenbildes gesehen haben. Bei Säurevergiftungen haben wir keine spastische Er-cheinungen gesehen. Dies bedeutet natürlich nicht, dass nach Einnehmen iner Säure an dem Magen kein Spasmus aufzutreten pflegt, sondern nur las, dass so ein Fall nicht zur Untersuchung gelangt ist. Die Röntgen-ilder der spastischen Magenveränderungen werden wir bei der Be-prechung der mit Lauge Vergifteten später verführen.

Infolge ernsterer Säureätzungen sind an den Magen Vernarbungen ntstanden. Die Stellen der Vernarbung lagen in überwiegender Zahl in der Pylorus-Gegend, seltener haben wir sie am Magenkörper gesehen. Da die Vernarbung nur ein Ausdruck der in die Tiefe dringender Säure-wirkung ist, unabhängig von der Qualität der eingenommenen Säure, kommt sie nach der Einnahme jedweile Säure zustande. Wir haben sie ebenso nach Vergiftungen mit Salzsäure, Ameisensäure, Schwefel-säure usw. beobachtet.

Die Vernarbungen verändern den Hohlraum des Magens, und damit zusammen natürlich auch seine Form, asymmetrisch. Infolge der mit der Vernarbung zusammengehender Schrumpfung erleiden auch die Lage-verhältnisse der einzelnen Teile des Magens zueinander grosse Verschie-bungen.

Im Allgemeinen sehen wir, dass der Magen verkleinert ist, hoch liegt, die kleine Kurvatur verkürzt und schneckenartig nach oben gewunden ist und der antrale Abschnitt und der Pylorus nach oben und nach links gezogen sind. Die Entleerung ist verhindert, weswegen die intermediäre Schicht hoch ist. An den von den Vernarbungen starren Wandteilen schreitet die Peristaltik nicht fort, oder wird auffallend kleinwellig. In-folge der oben auseinandergesetzten Ursachen entstellen die Vernarbungen zumeist den antralen Abschnitt: der antrale Abschnitt verschmälert sich stark und seine Grenzlinien sind oft uneben und zerfressen.

Am frühesten haben wir nach Salzsäure-Einnahme — und zwar am 9. Tage — eine antrale Vernarbung nachgewiesen (Bild 6). Der Magen-körper zeigte keine besondere Veränderung, sein Form war normal. Der antrale Abschnitt war röhrenformig verschmälert, an der kleinen und grossen Kurvatur sah man eine seichte, kleinwellige Peristaltik. Das Kontrastmittel durchschiesste beinahe den antralen Abschnitt, eine in-tensive Füllung gelang deshalb nicht. Wegen der schnellen und ständigen Entleerung des Magens war auch das Duodenum ständig voll. Nach einer Salzsäure-Vergiftung haben wir bei einem anderen Fall am 16. Ta-ge schon die Zeichen ausgesprochener und tieferdringender Vernäderun-

Bild 7. Bild 8.

Bild 7. Salzsäure-Vergiftung. Antrumvernarbung. 16 Tage nach der Vergiftung: der antrale Teil ist im ganzen schmaler, zeigt einen horizontalen Ablauf. Die Entleerung ist beschleunigt, der Bulbus Duodeni ist ständig gefüllt.

Bild 8. Salzsäure-Vergiftung. Hochgradige Antrumvernarbung. 13 Tage nach der Vergiftung: der Magen ist ausgesprochen erweitert, atonisch, in ihm gewaltige Flüssigkeitsmenge. Von dem antralen Abschnitt ist nur ein ganz kurzer ausgespitzter Teil übrig geblieben. Entleerung fehlt.

gen gefunden (Bild 7). Der Magen im Ganzen ist kleiner, sein Körper ist ungefähr ziegelsteinförmig, die intermediäre Schicht ist zwei Finger breit und die grosse Kurvatur ist gezähnt, besonders in der Gegend der Pars media. Der antrale Abschnitt ist im Ganzen schmaler, zeigt einen horizontalen Ablauf, deshalb ist der durch den auf- und absteigenden Schenkel geschaffene Winkel zum rechten Winkel vergrössert. Die Entleerung ist beschleunigt, der Bulbus und der hufeisenförmige Teil des Duodenum sind ständig gefüllt. Infolge starker Vernarbung kann der antrale Abschnitt fast vollkommen verschwinden. So war am 18. Tage nach Salszäure-Einnahme eigentlich nur der Pars descendens und Pars media des Magens sichtbar. Der antrale Abschnitt fehlte fast vollkommen und nur ein schmaler zapfenförmiger Teil, der blind endet, war von ihm übergeblieben. Eine Entleerung haben wir auch nach 24 Stunden nicht beobachtet, hier hat sich also schon eine vollkommene Pylorus-Stenose entwickelt. Die Erweiterung des Magens pflegt dann ausgespro-

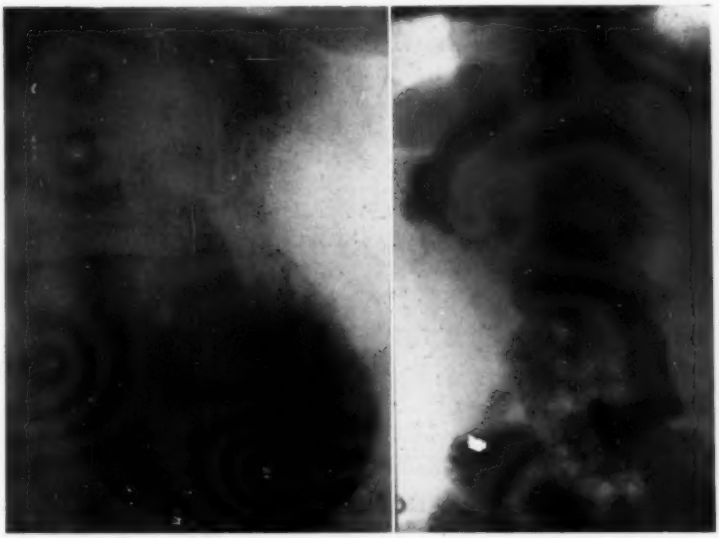


Bild 9. Bild 10.

Bile 9. Schwefelsäure-Vergiftung. Motorische Insuffizienz II. Grades wegen antralen Vernarbung. 10 Tage nach der Vergiftung: der Magen ist gewaltig erweitert, in ihm viele Flüssigkeit.

Bild 10. Chlorzink-Vergiftung. Schrumpfmagen. 7 Woche nach der Vergiftung: der Magen ist zu einer unregelmässigen, starren Röhre geschrumpft. (Seite verkehrt!)

chen sein, wenn die Stenose während einer längere Zeitspanne und stufenweise sich entwickelt hat. Bei einer unserer Kranken sind schon am 4. Tage nach der Salzsäure-Vergiftung die Zeichen der Entleerungshemmung aufgetreten, die sich am 13. Tage bis zum vollen Verschluss gesteigert haben. (Bild 8.) Von dem antralen Abschnitt ist auch hier nur ein ganz kurzer, ausgespitzter Teil geblieben. Der Magenkörper ist ausgesprochen erweitert, atonisch, in ihm hat sich eine gewaltige Menge Flüssigkeit gesammelt. Die Erweiterung des Magens jedoch kann auch in viel kürzerer Zeit bedeutend sein, wie wir das am 10. Tage nach Schwefelsäurevergiftung gesehen haben. (Bild 9.) Die Sperrung ist noch nicht vollkommen, aber wie erwähnt, ist dies eben eine Bedingung der grösseren Erweiterungen.

Zur Charakterisierung dessen, in welchem Grade die Vernarbung und die mit dieser einhergehende Schrumpfung die Form des Magens entstellen kann, demonstrieren wir einen am 30. Tage nach Chlorzinkeinnahme untersuchten Fall. (Bild 10.) Der Magen, beziehungsweise sein

Bild 11.

Bild 12.

Bild 11. Lauge-Vergiftung. 9 Tage nach der Vergiftung: stark geschwollene Falten mit zickzackigem Ablauf. Die Schleimhautplastik ist vollkommen zerrissen.
Bild 12. Lauge-Vergiftung: 20 Tage nach der Vergiftung: am oberen Teil des Magens körnige Zeichnung (Granulation).

Rest, liegt hoch, sein Hohlraum ist zu einem fingerbreiten Kanal zusammengeschrumpft und seine Wände sind starr. Der Magenstumpf ist durch unebenrandige Kontraststreifen, in denen eine bohnengrosse Erweiterung eingeschaltet ist, mit dem stark erweiterten, nach links gezogenen und nach oben gehobenen Bulbus Duodeni verbunden, der gleich am Anfang der Untersuchung überfüllt ist. Die Konturen des Bulbus sind übrigens heil. Der Pars horizontalis sup. duodeni hat wegen der hohe Lage des Bulbus einen steilen Ablauf.

Das Röntgenbild der nach Laugevergiftung entstandenen Magenverletzungen ist im allgemeinen gleich mit der nach Säurevergiftung entstandenen. In leichteren Fällen haben wir nur eine starke Schwellung der Schleimhautfalten und eine Zahnung der grossen Kurvatur gesehen. Im Allgemeinen beherrscht diese starke Schwellung der Falten die Bilder. Wegen der starken Einwölbung der Falten verschwindet stellenweise das Relief fast vollkommen, nur die hie und da sich zeigende Faltenfürchen deuten es an. Gewöhnlich haben wir dies am oberen Teil des Pars descendens beobachtet, aber in einem Fall auch an antralen Abschnitt gesehen. Die Schleimhautplastik ist manchmal vollkommen zerrissen. (Bild 11.) Die gewaltig geschwollenen Falten haben einen zickzack Ablauf gezeigt und nichts hat uns an die sich harmonisch liegenden Faltenlinien des normalen Magens erinnert. Nach Laugevergiftungen ha

Bild 13. Bild 14.

Bild 13. Lauge-Vergiftung. 3 Tage nach der Vergiftung: der Magenkörper ist durch einen engen spastischen Kanal in einem kleineren oberen und in einem grösseren unteren Teil geteilt und wiedergibt so ein Bild des Kaskaden-Magens.

Bild 14. Lauge-Vergiftung. Spasmus am Magen und am Duodenum. 2 Monaten nach der Vergiftung: an der Seite der grossen Kurvatur des antralen Abschnitts ist eine fingerspitzengrosse, scharfrandige Einziehung. Der hufeisenförmige Teil des Duodenums ist ständig gefüllt, Pars horizontalis sup. ist ausgesprochen erweitert.

ben wir also ein charakteristisches Relief nicht gesehen. Wir haben nur einen Fall erwähnenswert gefunden. (Bild 12.) Die Kranke ist am 10. Tage nach der Vergiftung zur Untersuchung gelangt. Die Falten waren im Allgemeinen plump gewunden. An dem oberen Teil des Corpus waren zahlreiche kleinere und grössere Körnchen zu sehen, die sich an einer Stelle dünner, an anderer dichter gruppiert haben. Diese Zeichnung (granulatio) ist ein ziemlich selten vorkommenden Reliefbild. Es kommt gewöhnlich vor in Fällen von Gastritis hypertrophica und Gastritis verrucosa. Sein Entstehen wird dadurch erklärt, dass die an der Magenwand haftenden Schleimkügelchen sich mit den Kontrastmittel mischen. Eine ähnliche, aber viel grössere Zeichnung sieht man in dem Fall des »état mamelloné» und in dem der hochgradigen Speiseröhreerweiterung; bei dem letzteren wird die körnige Zeichnung, die manchmal geradezu eine Polypose nachahmt, durch die Vermischung der stagnierenden Speise, der Luft, des Schleimes, und des Kontrastmittels verursacht.

Bild 15. Bild 16.

Bild 15. Lauge-Vergiftung. Ausgedehnte Vernarbung am Magen. 3 Wochen nach der Vergiftung: der Magen ist im ganzen kleiner, hochliegend. Der antrale Abschnitt ist zu einer schmalen, schroffen Röhre mit steilen Ablauf verengt.

Bild 16. Lauge-Vergiftung. Vernarbung an der Pars media. 2 Wochen nach der Vergiftung: die Pars media fehlt vollkommen, von dem antralen Abschnitt ist nur eine schmale, schroffwandige Röhre geblieben.

Vollständigkeitshalber erwähnen wir noch, dass die Schleimhautaufnahme des mit $KMnO_4$ vergifteten Falles zeigte ebenso nur das partielle Verschwinden des Reliefs.

In schwereren Fällen haben wir schon spastische Erscheinungen gefunden. Einen am oberen Teil des Magens bestehenden Spasmus hat das Bild des Kaskaden-Magens treu wiedergegeben (Bild 13). Der wegen des Spasmus zustande gekommene enge Kanal teilt den Magenkörper in zwei Teile: in einen kleineren oberen und in einen grösseren unteren. Der Mageninhalt gelangt wasserfallartig aus dem oberen Teil in den unteren. Wir haben erwähnt, das die spastischen Erscheinungen durch ihre Unbeständigkeit charakterisiert sind, beziehungsweise dadurch, dass sie auf die Wirkung von krampflösenden Mitteln oder nach einer gewissen Zeit im Verlauf der Heilung verschwinden. Bei einer Kranken haben wir zwei Wochen nach der Laugenvergiftung an dem antralen Abschnitt einen Spasmus nachgewiesen, der die Antrumbildung asymmetrisch gestaltet hat. Bei der neueren nach weiteren zwei Wochen wiederholten Untersuchung wurde die Antrumbildung wieder symmetrisch und der Spasmus war vollständig verschwunden.

Bild 17.

Bild 18.

Bild 17. Lauge-Vergiftung. Hochgradige Antrumvernarbung. 18 Tage nach der Vergiftung: der Magen ist im ganzen kleiner, kleine Kurvatur verkürzt, von dem antralen Abschnitt nur eine fadendünne Röhre geblieben.

Bild 18. Lauge-Vergiftung. Antrumvernarbung. 3 Wochen nach der Vergiftung: der Magenkörper ist ausgesprochen erweitert, der antrale Abschnitt ist zu einer unebenrandigen schmalen Röhre verengt.

Spasmen können gleichzeitig auch an mehreren Stellen des Magens erscheinen und so ernste Symptome verursachen, dass ein chirurgischer Eingriff notwendig werden kann. Eine unserer Kranken ist nach zwei Monaten nach der Laugeneinnahme wegen starker krampfartiger Schmerzen in der Magengegend und öfteres Erbrechen zur Untersuchung gekommen. Die Kranke hat wegen Speiseröhreverengerung eine Magenfistel bekommen. Das Anfüllen wurde durch die Magenfistel durchgeführt. (Bild 14.) An der Seite der grossen Kurvatur des antralen Abschnittes des Magens ist eine fingerspitzengrosse, scharfrandige Einziehung. Das Duodenum ist kappenförmig, an seinen Konturen sind keine Veränderungen sichtbar. An dem hufeisenförmigen Teil des Duodenum zeigt sich während der Untersuchung eine heftige Peristaltik und Antiperistaltik, der hufeisenförmige Teil des Duodenum ist ständig gefüllt und sein Pars horizontalis inferior ist ausgesprochen erweitert. Der Spasmus ist also in diesem Fall an der grossen Kurvatur und am Duodenum gleichzeitig aufgetreten.

Die Vernarbungen verursachen ebenso Formentstellungen am Magen, wie wir dies nach den Säurevergiftungen gesehen haben. In unserem

Bild 19. Bild 20.

Bild 19. Lauge-Vergiftung. Narbige Duodenumverengerung. $1^1/_2$ Jahre nach der Vergiftung: der distale Abschnitt des Pars descendens des Duodenums ist verschmälert, die oralen Teile sind erweitert.

Bild 20. Lauge-Vergiftung. Narbige Duodenumverengung. 4 Wochen nach der Vergiftung: der Bulbus Duodeni ist zusammengedrückt, kastanienförmig; der hufeisenförmige Teil bleistiftdünn verengt.

Material haben sich die Vernarbungen folgendermassen verteilt: Corpus 4, Antrum 11, Duodenum 2 Fälle.

Eine solche Röntgencharakteristik der Formveränderungen, die die nach Laugenätzung entstandene Vernarbungen von den nach Säureätzung entstandenen unterschieden hätte, konnten wir nicht feststellen. Wie auch die obenerwähnte zahlenmässige Zusammenstellung zeigt, wird auch nach Einnahme einer Lauge der antrale Abschnitt an öftersten verletzt. Infolge der Schrumpfungen entstehen die allerbizarrsten Bilder. (Bild 15.) Drei Wochen nach der Vergiftung ist der Magen im Ganzen kleiner ind liegt höher. Der antrale Abschnitt ist zu einer schmalen, starren, bogenförmig verlaufenden Röhre verengt, deren Konturen an der grossen Kurvatur uneben sind. Die kleine Kurvatur ist verengt. Zwischen der Pars media und dem antralen Abschnitt an der Seite der grossen Kurvatur zeigt sich eine beständige, scharfrändige, tiefe Einziehung. Die Entleerung ist stürmisch, das Duodenum und die Dünndärme füllen sich ständig. Manchmal entstehen wegen der Schrumpfungen ausgedehnte Defekte, besser gesagt Defekte nachahmende Volumenverkleinerungen. (Bild 16.) Der Pars media fehlt vollkommen, von der

antralen Abschnitt ist nur eine ganz schmale, den Ablauf der kleinen Kurvatur folgende starrwandige Röhre geblieben, durch die das Duodenum ständig angefüllt wird. Bei einem unserer in der vierten Woche nach der Vergiftung beobachteten Fälle, bei dem wegen der gleichzeitig bestehenden Speiseröhrenverengerung auch eine Gastrostomie ausgeführt wurde, war der Magen schon stark erweitert, besonders in der Richtung seines Horizontal-Durchmessers, die kleine Kurvatur ist verkürzt. Alle diese Veränderungen zusammen mit dem narbigen antralen Abschnitt haben den Magen am meisten einer Teekanne ähnlich gestaltet.

Wir haben eine totale Pylorus-Stenose in vier Fällen gesehen. Bei einen 18 Tage alten Fall (Bild 17) ist der Hohlraum des Magens kleiner als gewöhnlich, die intermediäre Schicht ist zwei Finger breit, die kleine Kurvatur stark verkürzt, von dem antralen Teil ist nur ein ungefähr 2 cm langes Stück geblieben, das in die Höhe gezogen ist. In einem anderen 23 Tage alten Fall war der Magenkörper dünndarmweit, schmal, und endet an seinem unteren Pol blind. Den antralen Abschnitt deutete nur eine warzenartige Anschwellung an. In beiden Fällen war der Verschluss vollkommen; eine Entleerung haben wir auch nach 24 Stunden nicht beobachtet. Die sich langsam entwickelnde Verschliessung verursacht eine ausgesprochene Erweiterung. (Bild 18.) In der 3. Woche nach der Vergiftung ist der Corpus gewaltig erweitert und der zu einer im unregelmässigen Zick-Zack ablaufenden starren Röhre umgewandelte antrale Abschnitt geht wegen der Verkürzung der kleinen Kurvatur beinahe von der Mitte des Pars descendens aus.

Die auf Grund einer Verätzung entstandenen Duodenum-Vernarbungen verdienen eine besondere Beachtung. Bekanntlich ist es ein ziemlich seltener Fall, dass der ätzende Stoff in solcher Konzentration in die Därme gelangt, dass dort noch tiefdringende Verletzungen zustande kommen könnten. In der Literatur gibt es sehr wenig diesbezügliche Veröffentlichungen.

Wir halten von diesem Standpunkt aus die zusammenfassende Veröffentlichung Balázs's vom Jahre 1934 für die allerkompetenteste, in der er auf Grund eines sehr grossen Materials (2,134 Fälle) das Schicksal der Lauge-Vergifteten behandelt. Von diesem Kranken-Material sind 100 Fälle zur Sektion gebracht und es wurde festgestellt, dass im 15 % der Fälle Verletzungen an den Därmen unterhalb des Pylorus (Duodenum, Jejunum und Colon) vorhanden waren. Die Verletzung war um so oberflächlicher und umschriebener je weiter sie von Pylorus entfernt lag. Eine Verletzungsmöhlichkeit des Duodenums gehört also zweifellos zu den Tatsachen. Es ist jedoch schwer eine Erklärung dafür zu finden. Höchstens gibt uns das irgendeine Anleitung, dass alle unsere beschriebenen Fälle nach Laugevergiftungen beobachtet wurden, hingegen nach Säurevergiftungen keine Duodenum-Verletzung vorhanden ist. Dieser

Umstand müssen wir eine entscheidende Bedeutung beimessen. Wie wir wissen, ist die Pylorus-Funktion durch den Mehring'schen Reflex geregelt. Eine sauere Reaktion schliesst, eine laugige öffnet diesen. Nach dieser Überlegung ist es gar nicht so überraschend, dass eine Verletzung des Duodenums nur nach der Einnahme einer Lauge gesehen wurde, denn eben da ist sie zu erwarten. Diese theoretischen Erwägungen sind durch die Tierversuche TESTA's gestützt. Nach den Versuchen in der I. Phase schliesst sich nach der Einführung der Lauge der Pylorus vollkommen, öffnet sich aber nach einer gewissen Zeit (II. Phase). Die gleichzeitig eintretende Peristaltik und Antiperistaltik drückt den laugigen Inhalt teilweise gegen die Cardia, aber teilweise auch gegen das Duodenum und dieser verursacht dort Verletzungen (Duodenitis, Spasmus, Vernarbung). Bei zwei von unseren Fällen haben wir eine Vernarbung des Duodenums nachgewiesen. Die eine Kranke hat vor $1^1/_2$ Jahren eine Laugevergiftung erlitten. Seit ein paar Wochen ist Gelbsucht aufgetreten. Nach der Untersuchung ist der antrale Abschnitt verschmälert und asymmetrisch (Bild 19) aber die Peristaltik bewegt sich über ihn fort. Der Bulbus duodeni ist regelmässig ausgefüllt und kappenförmig. Der Pars horizontalis sup. des Duodenums und der proximaler Abschnitt des Pars descendens sind bedeutend erweitert, dagegen ist der distale Abschnitt des Pars descendens verschmälert.

In den anderen Fall (Bild 20) war der Magenkörper weiter und glattrandig. Der antrale Abschnitt ist schmal, füllt sich blass an, das Kontrastmittel ist durch ihn durchgelaufen. Der Bulbus duodeni ist zusammengedrückt, kastanienförmig, scharfrandig. Das Duodenum in seinem ganzen Ablauf ist ebenso scharfrandig und zur Dicke eines Bleistiftes verengt.

In Anbetracht dessen, dass wir nach dem obenerwähnten eine Verletzung des Duodenums nur nach Laugenvergiftungen gesehen haben, können wir diesen Umstand zur Differential-Diagnose gegenüber den Säurevergiftungen benützen.

Die angeführten Bilder der Vernarbungen des Magens verätzenden Ursprungs demonstrieren uns ohne weiteres die grosse Ähnlichkeit, die zwischen ihnen und der Vernarbungen des Magens anderen Ursprungs besteht. Diese aussergewöhnliche Ähnlichkeit erschwert sehr, ja macht sogar in den meisten Fällen eine Differential-Diagnose gegenüber den durch peptische Geschwüre verursachten Vernarbungen des Magens unmöglich, sowie gegenüber den mit einer Bindegewebe-Proliferation und Schrumpfung einhergehende Formen des fibrösen Karzinoms, der Tuberkulose, des Lues, der Lymphogranulomatosis, der Aktinomykosis und der lymphatischen Leukämie. Ein jeder von den angeführten Prozessen kann — und sogar mit besonderer Vorliebe am antralen Abschnitt des Magens — die obenerwähnten Formveränderungen zustande bringen.

Eine Differentialdiagnose ist eben deshalb nur unter Einbeziehung anderer Umstände möglich, so wie klinische Symptome, Alter, serologische Reaktion, Allgemeinbefinden usw. Die allerwichtigste und entscheidende ist jedoch natürlich, wie wir schon bei der Besprechung der Speiseröhren-Vernarbungen betont haben, die Anamnese. Ihre Aufdeckung bis in die Einzelheiten ist bei jeder narbiger Veränderung des Magens unerlässlich, weil man damit rechnen muss, dass die Kranken die Ursache der in selbstmörderischer Absicht oder zufällig erlittenen ätzenden Vergiftungen aus Schamgefühl oder Vergesslichkeit verschweigen. Mit Ausnahme des zuletzt Erwähnten erleichtert die Aufgabe des Untersuchers auch jener Umstand, dass ausser dem Geschwür und Krebs die angeführten anderen Prozesse ziemlich selten vorkommen. Endlich macht in frischen Fällen das eventuelle Vorhandensein einer charakteristischen wabenförmigen Zeichnung die Diagnose einer Säurevergiftung sehr wahrscheinlich.

ZUSAMMENFASSUNG

Bei Laugenvergiftungen sind die Verletzungen des Verdauungstraktus im Allgemeinen schwerer und ausgedehnter als bei Säurevergiftungen. Sowohl die Speiseröhre, als auch der Magen wird gewöhnlich verletzt. Es kommt jedoch oft vor, dass nur die Speiseröhre verletzt wird, dagegen am Magen keine nachweisbaren Veränderungen entstehen.

Bei einer Säurevergiftung entstehen häufig an der Speiseröhre keine nachweisbaren Veränderungen und nur der Magen wird verletzt; gleichzeitig kommt eine isolierte Pylorusverletzung häufiger vor, als bei Laugevergiftungen.

Die isolierten Pylorus-Verletzungen werden durch den verminderten Tonus des Magens und durch die zwischen den Ätzmitteln bestehenden Viscositäts-Unterschiede ermöglicht. Auf die Einwirkung einer Säure hin kann an der Magenschleimhaut eine eigentümliche »wabenartige Zeichnung» entstehen. Die Verletzungen des Duodenums sind selten und der Verf. hat sie nur nach Laugevergiftungen beobachten können.

Die Differentialdiagnose der Vernarbung des Magens verätzenden Ursprungs gegenüber Vernarbungen anderen Ursprungs ist ausschliesslich auf Grund des Röntgenbildes nicht möglich.

SUMMARY

The effects of ingestion of alkaline poisons are usually more dangerous and severe and more widespread in the gastro-intestinal tract than are those of acid poisons. Usually both the esophagus and the stomach are involved. However, it may often happen that only the esophagus is affected and the stomach shows no changes. With acid poisons the esophagus is commonly not involved and the damage is confined to the stomach. It is also more common for an isolated pyloric scar to be caused by acids than by alkalis. The pyloric scars are due to the lowered tone of the stomach and by the altered viscosity of its contents. After ingestion of an acid poison the mucosal pattern of the stomach may show a »honeycomb» appearance. The duodenum is seldom

involved in the case of acid and the author has only seen lesions here after alkali poisoning. It is not possible by roentgenological methods to differentiate between the scars due to acid or alkali poisoning and those due to other causes.

RÉSUMÉ

Dans les empoisonnements par la soude caustique les lésions du tractus digestif sont en général plus graves et plus étendues que dans ceux par les acides. Aussi bien l'œsophage que l'estomac sont habituellement blessés. Cependant il arrive souvent que seul l'œsophage le soit, et qu'en revanche il ne se produise pas d'altérations démonstrables dans l'estomac. Dans un empoisonnement par l'acide l'œsophage, fréquemment, ne présente aucune lésion qu'on puisse mettre en évidence et seul l'estomac est blessé; en même temps une lésion isolée du pylore survient plus souvent qu'avec la soude caustique. Ce qui rend possibles les lésions isolées du pylore, c'est la modification du tonus de l'estomac et les différences de viscosité qui existent entre les divers caustiques. Sous l'effet d'un acide on peut voir apparaître un curieux «dessin alvéolaire» de la muqueuse gastrique. Les lésions du duodénum sont rares, et l'auteur n'a pu les observer qu'après des empoisonnements par la soude caustique. Il n'est pas possible de faire uniquement d'après les images radiologiques le diagnostic différentiel entre les cicatrices stomacales dues à des caustiques et celles d'autre origine.

LITERATUR

1. Assmann: Klinische Röntgendiagnostik der inneren Erkrankungen. 1934.
2. Balázs: Laugenvergiftungen (Selbstmorde). Sammlung von Vergiftungen. B. 5. 1934. — Erfahrungen auf dem Gebiet der Laugenvergiftungen bei Erwachsenen. Ärztliche Wochenschrift. 1928
3. Bock und Hin: Postkaustische Magenverätzungen. Röpra 3. 1931.
5. Eckerdt: Durch Laugenvergiftungen verursachten pathologisch-anatomische Veränderungen in den Verdauungstraktus. Ärztliche Wochenschrift Nr. 11.
5. Forssell: Fschr. Rtgstr. Kongress H. 16. 1935.
6. Galdau und Popp: Die postkaustischen Magenverätzungen. Fschr. Rtgstr. B 37.
7. Mehnert: Über die klinische Bedeutung der Oesophagus- und Aorten-Variationen. Arch. f. klin. chir. B. 58.
8. Udvardy: Röntgendiagnostik der inneren Erkrankungen. 1942.

FROM THE ROENTGEN DEPARTMENT OF HALMSTAD HOSPITAL, SWEDEN (HEAD: DR. BENGT LILJA, M. D.) AND THE ROENTGEN DEPARTMENT OF SERAPHIMER HOSPITAL, STOCKHOLM, SWEDEN (HEAD: PROFESSOR ERIK LYSHOLM †)

THE TENTORIAL PRESSURE CONE, ITS SIGNIFICANCE AND ITS DIAGNOSIS THROUGH DISLOCATION OF THE CALCIFIED PINEAL BODY[1]

by

Bengt Lilja, M. D.

Neurological symptoms occur not infrequently in expansive intracranial processes originating from parts of the brain which lie at a considerable distance from the seat of disease. In this manner a far too prolific and confusing flora of symptoms can arise which cannot be concentrated on a uniform and limited focus in the brain. During recent years many of these hitherto obscure clinical symptoms have found an explanation in the displacement of and changes in shape of the brain substance. Signs of disease which, formerly, were thought to be caused by the general brain pressure as such have, with the knowledge of these changes, got a more local character. The observations are now well substantiated and are an object of growing interest in literature. JEFFERSON (1938) speaks of »the discovery of a gross mechanical phenomenon», and TÖNNIS (1938) considers this question as being »von geradezu fundamentaler Bedeutung». SCHWARZ and ROSNER (1941) write: »The early recognition of this dangerous complication is demonstrated to be as important as it is practical.»

The intention of this paper is to give a brief survey of our knowledge of the displacement of the brain substance and to compare the pathoanatomical, clinical and experimental observations appearing in literature with those published by the author in 1939 concerning this displacement as is demonstrated roentgenologically by the dislocation of the calcified pineal body in tumours of the brain. A resumé will also be given here of the author's former work besides which a simplified method of de-

[1] Submitted for publication, Sept. 21, 1947.

termining the position of the calcified pineal body, intended for practical use, will be described.

The inner and outer fluid spaces within the cranium play a dominating part as reserve spaces for the brain substance during increased pressure, especially the subarachnoidal cisterns which are described as being six in number *i. e.* the basal, ambiens, cerebello-medullaris or magna, the pontomedullaris, the interhemispherica and the sylvian fissure.

The greatest clinical attention has been called for by a postero-inferior displacement of the brain substance with a filling out of the large basal subarachnoidal cisterns. In this way changes in shape can occur, known as cerebellar or occipital pressure cone and temporal or tentorial pressure cone. These can give characteristic and even alarming clinical symptoms.

As a sign of a displacement of the brain substance, a dislocation of the pineal body has been shown roentgenologically in the cases where a calcification here exists. A natural indicator of this sort, situated in the central part of the brain, can, if used in the right manner, give valuable information about the topographical conditions within the cranium. The dislocation of the pineal body, in most cases postero-inferiorly or laterally, also coincides well with the patho-anatomical, experimental and clinical observations concerning which we will first give some historical information before dealing more thoroughly with the change in position of the pineal body.

Cerebellar pressure cone, described by QUINCKE in 1906, has been found to be a frequent occurrence in tumours of the posterior cranial fossa. The brain substance is pressed down into the foramen magnum so that the tonsils and neighbouring parts of the little brain shoot down at this point like a cone-shaped formation, whereby a cistern puncture becomes impossible or risky. This pressure cone can cause bulbar symptoms to arise, either intermittently or continuously with initial pains in the neck, influence on the pulse, vomiting, opisthotonus and so on and it is especially feared as a cause of sudden death from respiratory paralysis. It would seem that the cerebellar pressure cone is of remarkably small significance in regard to the ventriculogram (ANTONI 1941).

ADOLF MEYER (1920) has under the name of herniation of the brain described the pressing of the brain substance into the incisura tentorii *i. e.* the temporal or tentorial pressure cone. This tentorial pressure cone will be dealt with more in detail as it has a special significance in regard to the displacement of the pineal body. As a rule the tent-like shape of the tentorium affords good protection to the delicate mesencephalon with important centres and peduncles carrying pyramidal

tracts. But in the expansive processes above the tentorium the contents are pressed downwards towards the incisura tentorii. Here is found the horse-shoe shaped cisterna ambiens surrounding the mesencephalon on the dorsal side and demarcated laterally by the fastening edge of the arachnoidea on the inferior side of the great brain following the free edge of the tentorium. The cisterna ambiens proceeds along both shanks of the horse shoe at the side of the mesencephalon and communicates in this way with the cisterna basalis on the ventral side. And so reserve space is found here which can be used in space-crowding processes in the cerebrum. It is principally the uncus gyri hippocampi, situated on the lateral border of the cistern next to the free edge of the tentorium, which is squeezed and, on post-mortem examination, one finds here an impression of the tentorial edge in the brain substance. For the most part the pressure is located laterally of the isthmus cerebri though at times more anterior or more posterior to it, unilaterally or bilaterally. A possible deviation of the ventricle system, especially of the aqueductus sylvii, can be shown ventriculographically (ANTONI 1941). Pictures of pathological preparations of this kind have been published by numerous authors such as ADOLF MEYER 1920, KERNOHAN and WOLTMAN 1929, JEFFERSON 1938, HASENJÄGER and SPATZ 1938, ANTONI 1941 and many others. In a sectional material of 100 brains with expansive intracranial processes above the tentorium, principally abscesses and tumours, SCHWARZ and ROSNER (1941) have discovered such tentorial grooves with herniation of the brain substance in no less than 83 cases. In most of them this tentorial groove has been different on both sides thereby causing distortion, compression and displacement of the numerous structures at the base of the brain. The splenium of the corpus callosum was also pressed downwards especially if the pressure had acted directly above the incisura. Cerebral abscesses invariably produce marked disturbances in the hippocampal region. Cerebellar pressure cone could only be shown in relatively few cases having a marked temporal pressure cone. SCHEINKER (1945) has examined 55 cases of herniation in the incisura tentorii from expansive supratentorial processes such as haemorrhages, tumours, abscesses and traumatic insults. He maintains that a herniation even includes the brain stem and would therefore call the displacement arising in this way, »transtentorial herniation of the brain stem». Owing to the displacement and the gradual plugging up of the incisura tentorii, a compression and strangulation of the small and medium-sized veins can also arise. This causes a congestion in the veins and haemorrhage in the brain stem which has been shown in histological preparations and often localized to the tissue around the sylvian aqueduct. If the incisura tentorii is plugged up, the pressure in the ventricles often becomes greater than the lumbar pressure (SMYTH and HENDERSON

1938). This makes a lumbar puncture risky in cases of herniation in the incisura tentorii.

The clinical picture of this pressure in the incisura tentorii is not yet defined but begins to crystallize itself.

By the increased pressure of an expansive process towards one side of the mesencephalon, it can be moved over to the other side so that the pedunculus cerebri here presses against the sharp edge of the tentorium cerebelli. This means that an incisure in the peduncle can take place with destructive tissue changes corresponding to the tentorial edge. In this way damages occur on the pyramidal tract with homolateral paralysis (KERNOHAN and WOLTMAN 1929). A similar case was published already in 1927 by GROENEVALD and SCHALTENBRAND.

In some cases an attack of general rigidity has occurred accompanied by cramp of the extensory muscles so that the condition resembles a decerebrate rigidity in cats (JEFFERSON 1938, RIESSNER and ZÜLCH 1940). In addition, disturbances in pupillary reaction and paralysis of the eye muscles have been shown through pressure against the mesencephalon.

Other authors have also wanted to assign more symptoms to this tentorial pressure cone such as severe paroxysmal headache, stiff neck, hyperthermia and vasomotorial disturbances (VINCENT, DAVID and THIÉBAUT 1936).

SCHWARZ and ROSNER (1941) have compared the clinical pictures of 43 cases of supratentorial tumour with pronounced temporal herniation with 21 cases of similar tumours without herniation. These authors would assign to the temporal herniation mainly the following symptoms: disturbances in conscience, anisocoria, stiff neck, paralysis of the eye muscles, cardio-respiratory and thermoregulatory disturbances, symptoms from the pyramidal tract and decerebrate rigidity.

ADOLF MEYER (1920) discovered hemianopsia in a case of supratentorial tumour which he considers was brought about by an injury to the arteria calcarina caused by pressure. Similar cases with injury of the arteria cerebri posterior and its branches have been shown by other authors as well (MOORE and STERN 1938, RIESSNER and ZÜLCH 1940). A case of blindness in an otogenic abscess in the temporal lobe is considered by ALLISON and MORISON (1941) to have originated from temporary occlusion by stretching and kinking of the posterior cerebral artery as well as, possibly, direct pressure from the edge of the tentorium.

There is also information about cases with tentorial pressure cone and haemorrhage in the mesencephalon and pons which ended fatally (VAN GEHUCHTEN 1937, MOORE and STERN 1938).

A dilatation of the ventricle system is even considered to be caused by pressure in the tentorial incisure (SCHWARZ and ROSNER 1941).

Displacement of the brain in the direction of the subarachnoidal cisterns can also cause a double pressure cone, both tentorial and cerebellar, and this happens rather frequently in supratentorial tumours (ADOLF MEYER 1920, JEFFERSON 1938, RIESSNER and ZÜLCH 1940), and it has even been observed in a case of infratentorial tumour in which a hydrocephalus was thought to be the cause of the tentorial pressure (JEFFERSON 1938).

Mesencephalic symptoms, cramps resembling decerebrate rigidity and signs of disturbances in the pupillary reaction and functions of the eye muscles have been found by RIESSNER and ZÜLCH, 1940, in a case of tumour of the little brain where the tumour pushed up through the tentorial incisure and evidently pressed against the mesencephalon. In this case the symptoms are thought to have been caused by this displacement of the brain substance from below upwards and thus in an opposite direction to the usual. In a case of status epilepticus, ANTONI (1941) has described an upward displacement of the little brain which had a groove caused by the edge of the tentorium. He characterizes this displacement as an upper cerebellar pressure. Hence ANTONI explains the angular, downward curving of the posterior part of the sylvian aqueduct, which was described by LYSHOLM (1935), as a characteristic sign of tumour of the little brain. Even a lateral widening of the posterior parts of the lateral ventricles can, according to ANTONI, be accounted for in this manner. Similar tentorial grooves on the dorsal side of the little brain have also been observed by SCHWARZ and ROSNER (1941) in tumours of the posterior cranial fossa.

In addition to these changes in position, the cerebellar pressure cone and displacements in the tentorial notch, one has observed similar displacements with a filling out of the other cisterns. WINKELBAUER (1928) has shown a displacement, laterally under the falx, of the inferior, medial part of the hemisphere whereby a downward pressure of the corpus callosum occurred on the tumour side. The filling out of the cisterna interhemispherica in this condition is specially emphasized by SPATZ and STROESCU (1934) and it has also been studied by HASENJÄGER and SPATZ (1938). This displacement, denoted by ANTONI (1941) as cingulecus from gyrus cinguli, which is situated in this region, is often revealed by the ventriculogram. ANTONI also emphasizes as being especially noteworthy, that the lateral ventricle can be in this way displaced downwards on the tumour side even though the tumour lies in a basal position such as in the temporal lobe. In hydrocephalus occlusus the distension often affects the anterior cornu to a marked degree and this appears to be explained by the fact that the brain substance can force its way out

here against the cisterna interhemispherica which has its greatest expansion just in front (RIESSNER and ZÜLCH 1940).

Paralysis of the abducens which CUSHING, in 1910, showed was an aberrant symptom, is thought to be connected with a filling out of the cisterna ponto-medullaris (HASENJÄGER and SPATZ 1938).

The cisternae fissurae sylvii can also be used as reserve spaces in expansion of the brain substance with displacement either back or front according to the position of the tumour. Change of position of the brain substance can be shown here by an impression caused by the lesser wing of the sphenoid bone (RIESSNER and ZÜLCH 1940).

Experimental investigations have been carried out by PERRET (1940) on cats. By injecting a substance, which clotted at body temperature, into the parietal lobe, he has produced a local expansion supratentorially. On post-mortem examination, it was found that a displacement of the brain substance had taken place with a filling out of the cisterna ambiens, a pressing down of parts of the brain under the tentorial edge and, in some cases, compression and displacement of the mesencephalon together with a cerebellar pressure cone with a filling out of the cisterna magna. A displacement of brain parts was also shown between the falx and the corpus callosum over to the opposite side with a filling out of the cisterna interhemispherica and a displacement of the median plane and the whole ventricle system to the opposite side as well.

Similar displacements with a filling out of the cisterns could also be shown in hydrocephalus in cats caused by direct injection into the ventricle system as well as by injections into the subarachnoidal and subdural spaces. One also found clinical signs in animals from the mesencephalon and medulla oblongata resembling those in man. One has therefore found an experimental basis for the mechanical displacement of the brain substance.

After these short notes about the development of our knowledge of matters concerning changes in shape and displacement of the brain substance from a clinical, patho-anatomical and experimental point of view which, later on, will be further illustrated by displacement of the pineal body, I will summarily set out some points of view concerning the mechanical happenings within the cranium during the development of expansive processes. The local changes in shape must not be confused with the general increase in intracranial pressure even though both processes are intimately connected with one another.

It has thus been shown that, in local expansion, the brain substance is pressed away in the direction where the surrounding brain substance yields most and is able to give way towards the reserve spaces found within the cavity of the cranium, whereby the differences in pressure are evened up. The brain substance makes use of every othe-

space which is available on account of the difference between the content of the cranium and its capacity. But the reserve spaces for the most part consist of the subarachnoidal cisterns, which are gradually filled out by the brain substance. They make a displacement of the brain substance possible in a sagittal direction *i. e.* posteriorly and inferiorly, which causes a tentorial pressure cone and possibly a cerebellar pressure cone as well. The cisterna interhemispherica makes a displacement also in a transverse direction possible in the manner stipulated by the position of the tumour and the nature and direction of the growing pressure. When the brain substance encounters hard edges such as the tentorium, the foramen magnum and even the lesser wing of the sphenoid bone and the falx, impressions or grooves arise which can bring about changes in the tissues.

As the brain is enclosed within the cranium, the development of a local expansive process leads gradually to an increase in the general pressure. The fluid content of the subarachnoid space and the amount of blood diminishes, all the cavities fill out and the tissue substances are pressed together. This transfer from local to general increase in pressure is, however, very complicated in nature, dependent as it is on an ensemble of powers of different values. Under the influence of the expanding process, for instance a tumour, secondary changes can develop, which further contribute to an increase of the pressure, such as hydrocephalus, circulatory disturbances and »Hirnschwellung», which REICHARDT (1919) showed was caused by colloidal disturbances in the brain substance carrying with it an increase in the volume of the brain in lesser or greater regions. In addition, the transmission of the pressure to the different parts of the brain substance is influenced by the anatomical division of the cranium into three different fossae as well as by the further division of the cavity by the falx cerebri and the tentorium cerebelli.

A displacement of the brain substance in a sagittal and frontal plane can be seen roentgenologically by determining the position of the pineal body in those cases, about 50 %, where a calcification can be shown here, if this dislocation is so significant that, having regard to the variability of the size of the cranium and technical sources of error, it can be established with scientific certainty or, at least, with a statistically calculated degree of probability.

It is worth while pointing out here that the pineal body, situated as it is immediately in front of the cisterna ambiens, is in a very biassed position for the occurrence of a dislocation as it follows the brain substance when it presses downwards and backwards in order to fill out the

cisterns around the mesencephalon. If a cerebellar pressure cone also occurs in a supratentorial tumour it would seem to enhance the possibility of a dislocation of the pineal body.

The conditions in infratentorial tumours are quite different. Here too, and above all here, a filling out of the cisterna magna takes place from the pressing brain substance, but in this case the tumour causes an expansion of the contents in the posterior cranial fossa. Even if the pressure from the anterior parts of the cerebrum increases on account of the development of a hydrocephalus a counter-pressure will be found in the posterior cranial fossa.

Displacement of the pineal body laterally was first shown by SCHÜLLER (1912). Experiments in determining the normal position of the pineal body in the sagittal plane on roentgen pictures were first made by VASTINE and KINNEY (1927), but their method offers no possibilities making scientifically based calculations of probability.

In 1939 LILJA advanced a method of determining the position of the pineal body which was based on statistic calculations in relation to the variability of the size of the cranium. A criticism of the methods previously used will also be found in this work together with a critical survey of the sources of error connected with measuring on roentgen pictures. The following account is based mainly on this work.

For an examination of the position of the pineal body, two projections at right angles are required, that is to say a frontal projection for examination of a possibly present lateral displacement and a lateral projection in order to determine the position in the median-sagittal plane. For photographing in frontal projection the patient was placed in the dorsal position and the tube was inclined 35° in the cranial direction. The side-view was taken on adjustment of the medial-sagittal plane of the cranium parallel, as far as possible, to the film. The pictures were taken with LYSHOLM's special apparatus for cranial examination, now generally used in Sweden and several other countries. The roentgen tube here is movable on a semicircular arc which can also be turned so that the distance between the focus and the film remains constantly at 65 cm. On similar tables of more recent construction this distance is a few cm greater. The distance from the table surface to the film is 4 cm. The tube can thus be moved in all directions, the shift being read on graduated scales. Pictures 1 and 2 illustrate the two projections used. By measuring the distances or radii from the pineal body to the wall of the cranium on the side view, one can determine the position in the sagittal plane and by measurements made on the frontal view one can see any possible lateral displacement.

Calcification of the pineal body can be shown in the roentgen pictures in about 50 % of the cases over the age of 20. In only 40 % of the

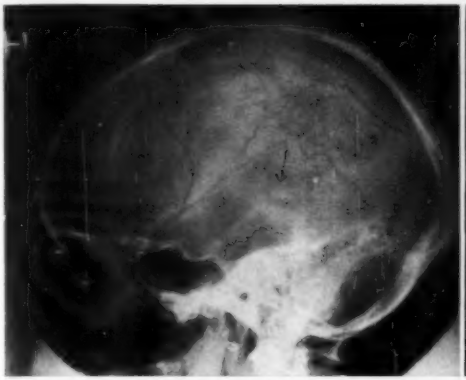


Fig. 1. Side-view of the cranium. Pineal body visible in normal position.

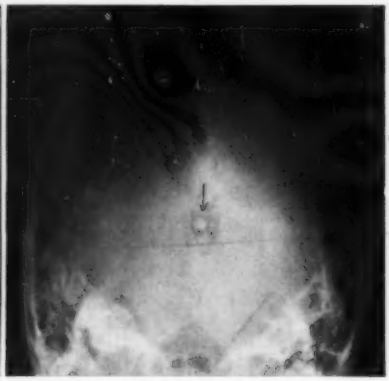


Fig. 2. Frontal view of the cranium. Pineal body visible in the midline.

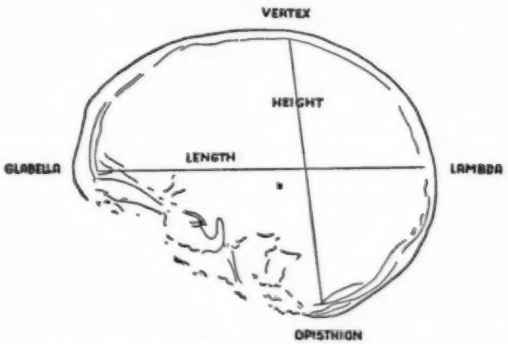


Fig. 3. The points used for determining the length and height of the cranium.

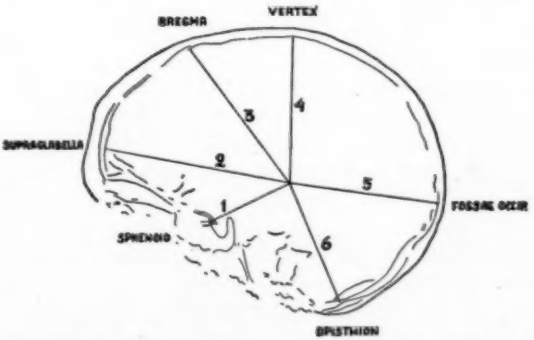


Fig. 4. The points which were used in measuring the distance to the pineal body.

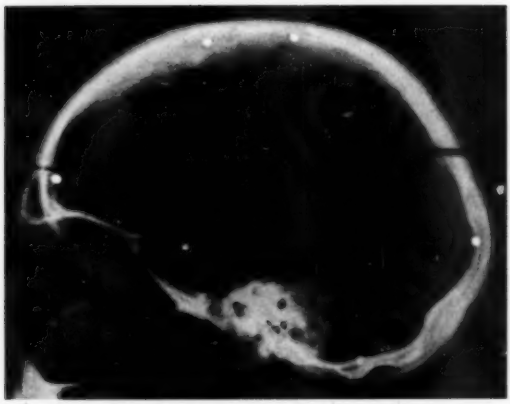


Fig. 5. Cranium with small shot fixed in the mid-line at points 1—6.

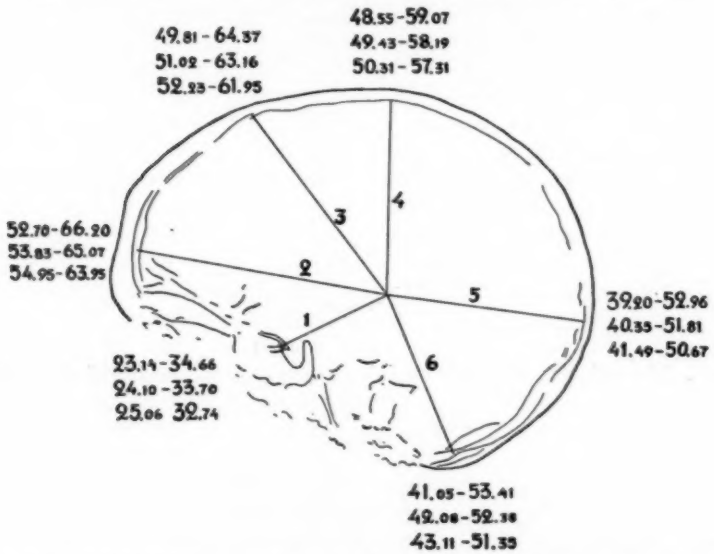


Fig. 6. Ranges of variation of the radii from the pineal body as percentages of skull length and skull height.

cases with calcification of the pineal body visible on the side-view was it possible to see it from the frontal view.

The variability of the measurements on the cranium has several causes. In the first place it depends on the fact that crania are of dif-

ferent sizes and the variability here is considerable. The length of a cranium on the roentgen picture taken in the manner described (Fig. 3) between the points marked on the figure, vary, as a matter of fact, from 16.3 to 21.4 cm and the height from 13.7 to 17.7 cm (calculated with $\pm$ 3 σ in a material of 200 skulls).

But the variability in the measurements on the roentgen picture is not merely stipulated by the difference in the size of the cranium. One must here take into account a variability stipulated by reasons which can be regarded as being technical and which can be classified into two groups, *i. e.* partly errors in measurement and partly photographic errors. Errors in measurement are partly due to the difficulties in locating exactly the craniometric points and partly to incorrect reading of the measuring instrument. Photographic errors depend on the fact that the roentgen method always involves an enlargement of the object reproduced, and this enlargement is dependent on the distances from focus to object and film and on the relation between these distances. Apart from this we find here another source of error arising from a moderate variation in the adjustment of the head, unavoidable in practical work.

Calculations of the value of these technical errors have been made from a series of experiments and have been found small in relation to the true variability in the size of the cranium. Only enlargement on the pictures seems here to be a factor to be taken into account. But this enlargement is, practically speaking, constant if the pictures are always taken at the same focal distance.

Meanwhile examinations have also been made regarding the mutual relation between the configuration and size of the head and the measurements which refer to the position of the pineal body. In this way, as was to be expected, it has been found that the established values of the radii from the pineal body proved to be affected by the varying sizes of the crania. Owing to this they were put in percentage relation to the length and height of the crania. One advantage of this index calculation is obvious. As the distances from the pineal body are expressed not directly but as percentages of the size of the cranium, the absolute values are only of secondary importance. It is the relation which is decisive. If the enlargement in photographing is not exactly the same — for instance owing to a difference in focal distance — even a large difference in focal distance, *e. g.* 10 cm, causes no difference in the percentage measurements of the radii from the pineal body.

As the radii from the pineal body are put in percentage relation with the measurements of each individual cranium, the method here used may be considered as having a fairly universal validity. On account of slight cranial asymmetries which frequently occur it may be difficult, in some cases, to decide whether a dislocation laterally actually exists.

FRAY (1936) states, however, that the pineal body in frontal pictures is situated in the central point of the largest transversal diameter of the cranium which agrees with the result of my own investigation.

For determining the position of the pineal body in the sagittal plane, 6 radii, spreading fanwise from the pineal body to the inside of the cranium, have been measured on a side view in 200 cases.

The following craniometric points were used for the six radii (fig. 4):

1. Sphenoid. The point at which the front border of the sella turcica (tuberculum sellae) intersects the median-sagittal plane. 2. Supraglabella. The upper limit of the median top point of the prominence which is situated in the lower portion of the frontal bone above the root of the nose. 3. Bregma. The median point at which the sagittal suture intersects the coronal suture. 4. Vertex. The highest point of the crown of the head situated in the median sagittal plane. 5. Median point corresponding to the deepest part of the occipital fossae. 6. Opisthion. The point at which the posterior margin of the occipital foramen intersects the median-sagittal plane.

The following craniometric points (Fig. 3) have been used for determining the length and height of the cranium.

Glabella. The median top point of the prominence which is situated in the lower portion of the frontal bone above the root of the nose. Vertex. See above. Lambda. The point at which the sagittal suture meets the two limbs of the lambdoid suture. Opisthion. See above.

The distance glabella—lambda expresses the length of the cranium, the distance vertex—opisthion its height. (Fig. 3.)

The radii from the pineal body (fig. 4) forwards to the sphenoid (1) and the supraglabella (2) and from the pineal body backwards to point 5 correspond in regard to the direction most closely to the length of the cranium and are calculated as percentages of the length of the cranium. The radii upwards to bregma (3) and to vertex (4) and downwards to opisthion (6) are mainly height measurements and are calculated as percentages of the height of the cranium.

On fig. 5 the craniometric points given here will be seen marked with small shot fixed in the midline.

Having calculated the measurements of the radii from the pineal body to the calotte as percentages of the length and height of the cranium, the values in the normal material appear from fig. 6.

The value for each radius calculated as percentage of the length and height of the cranium lies normally between the figures given in the bottom row of fig. 6. An observation outside the margin of figures in the bottom row (calculated with $\pm 2\,\sigma$) but within the margin of the figures in the middle row indicates a displacement of the pineal body but, however, in 1 case out of 22 such an observation is caused by chance *i. e.*

is a normal variant. The degree of certainty here does not allow of any extensive conclusions. An observation outside the margin of the figures in the middle row (calculated with $\pm 2.5\ \sigma$) but within the margin of the figures in the top row indicates a dislocation of the pineal body: the observation may, however, also here be caused by chance but only in 1 case out of 80. This margin of certainty is usually regarded as being satisfactory in practice (DAHLBERG 1926). If the percentually calculated value of a given radius lies outside the margin of the figures in the top row, it indicates that a value, diverging in such a way, occurs as a normal variant only in 1 case out of 370. (The figures given are thus calculated with $\pm 3\ \sigma$.) A degree of certainty such as this is considered as being fully satisfactory.

The following examples will illustrate the probability of the observations. The directly measured value of radius 1 is calculated percentually to the length of the cranium. Every measurement of radius 1 which is smaller than 23.14 % or larger than 34.66 % of the length of the cranium, accordingly has a probability of 1 : 370, that is to say, such a value will arise by chance only in 1 case out of 370 or in 0.27 % of the cases. For instance, for radius 4, an observation of 58.7 % of the height of the cranium falls outside the extent of variation in the middle row but within the extent of variation in the top row; this value consequently arises by chance only in 1 case out of 80. And finally, if radius 6, measured on the picture, is calculated percentually to the height of the cranium, and, in this manner, gets a value of 42.9 %, it indicates that the value arises by chance in 1 case out of 22 thus falling outside the degree of variation which is given in the lower row but within the degree of variation according to the middle row.

If, for the purpose of determining a displacement of the pineal body, one presumes that the value of the radii is outside $\pm 2.5\ \sigma$ it must be pointed out that a suchlike diverging value can be observed in a perfectly healthy person namely in 1 case out of 80. The probability is therefore small but not altogether absent that the value has arisen by chance. As it is therefore seldom that a displacement like this is a normal occurrence there is an overwhelming probability of its being caused by a pathological process. It is not possible, however, to proceed one step further and arrive at a numerical expression for the probability of its being either mere chance or abnormal. Therefore it is not possible to arrive at a relative figure between the number of displacements of pathological origin and those due to mere chance. An examination like this cannot be undertaken just because the material, which should be examined, has an undefined borderline and would include selected cases with different kinds of neurologic symptoms. The indications for roentgen examination are different in different clinics. It is, however, of con-

siderable help, when making a diagnosis, to obtain from these examinations a numerical expression of the general probability that an observed displacement is either due to chance or that it is abnormal. If one draws the margin outside $\pm 3\ \sigma$, the probability (1/370), that it is a matter of chance, is so small that it needs scarcely be noticed or, in other words, that the observation alone is, practically speaking, sufficient for diagnosing a pathological process. If, as here, one also avails oneself of the probability calculated at $\pm 2.5\ \sigma$, the deviation, calculated in this manner, must be made use of with greater regard to the other symptoms arising in brain tumours. When an observed displacement only goes outside $\pm 2\ \sigma$, it must be given a limited value as one knows that in 1 case out of 22 it is here a question of a normal occurrence.

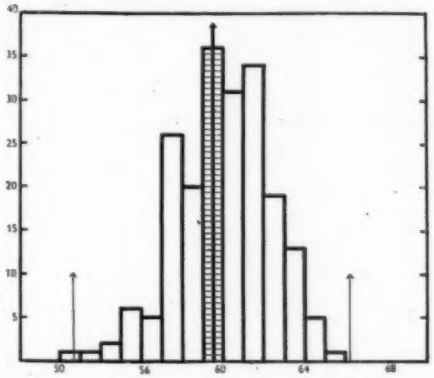
The question of the position of the pineal body should moreover be gauged from all sides and all the measurements should be considered and compared. If the radii upwards from the pineal body have too high a value the assumption gains in strength that a displacement of the pineal body is actually present if the radius downwards from the pineal body has too low a value. The same applies to the radii from the pineal body forwards and backwards. As a matter of fact it is the rule, in dislocation of the pineal body, that the measurements of the radii change in several directions so that, for instance, a high value on an upward radius corresponds to a low value on a downward radius. If only one radius shows a value which diverges from the ordinary, one has reason to judge the case with reservation as, in such a case, one may also weigh up the possibilities of there being a local change in the shape of the cranium.

The position of the pineal body has been determined in a material of 217 cases of operatively verified tumours from OLIVECRONA's clinic. The results are presented in graphic form on the following pages so that a better survey of the results may be obtained. Each radius from the pineal body has been illustrated by three graphic charts. The top picture on the page originates from the normal series (200 cases) and is included here for comparison with the pathological material. The cases with supratentorial tumours have been placed in one group and those with infratentorial tumours in another one as it has been shown that it is mainly the tumours above the tentorium which cause a displacement of the pineal body. Each group is illustrated by a graphic chart. The average in the *normal* series is shown on all pictures by columns marked with lines. The thin arrows on the sides mark the *normal* degree of variation calculated at $\pm 3\ \sigma$. As all the charts are of the same type, only the charts of four of the radii are represented here.

Radius 2. Pineal body—supraglabella.

The normal series, 200 cases.

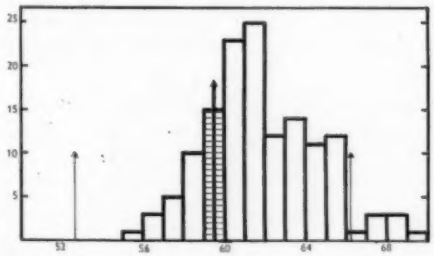
Number of cases.



Radius 2 as percentage of the length of the cranium.

Tumours above the tentorium, 139 cases.

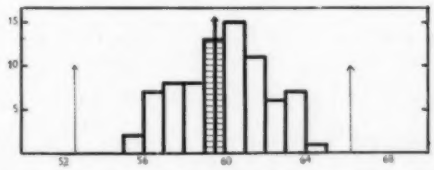
Number of cases.



Radius 2 as percentage of the length of the cranium.

Tumours below the tentorium, 78 cases.

Number of cases.

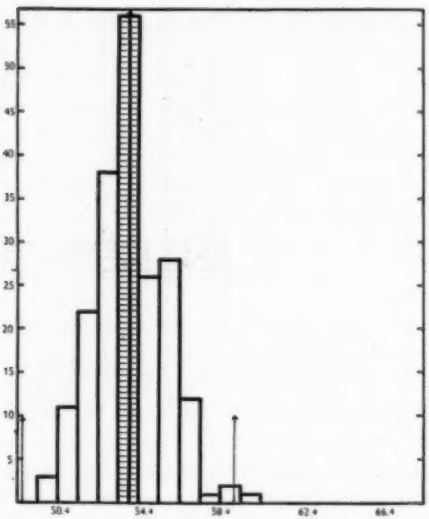


Radius 2 as percentage of the length of the cranium.

Radius 4. Pineal body—vertex.

The normal series, 200 cases.

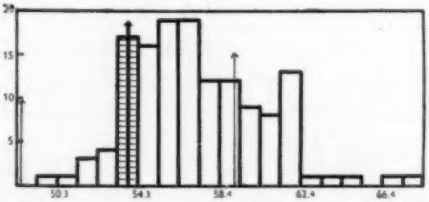
Number of cases.



Radius 4 as percentage of the height of the cranium.

Tumours above the tentorium, 139 cases.

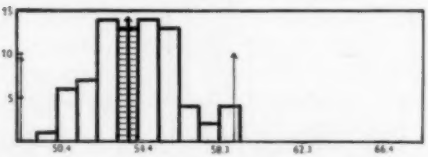
Number of cases.



Radius 4 as percentage of the height of the cranium.

Tumours below the tentorium, 78 cases.

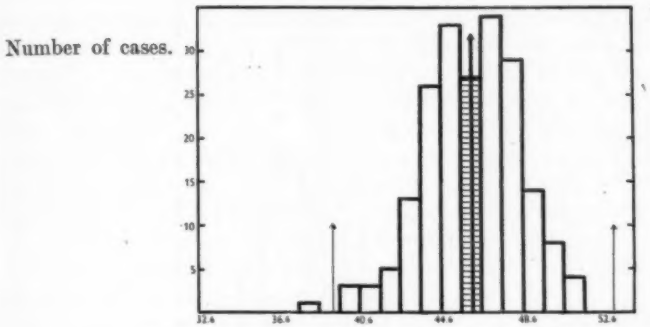
Number of cases.



Radius 4 as percentage of the height of the cranium.

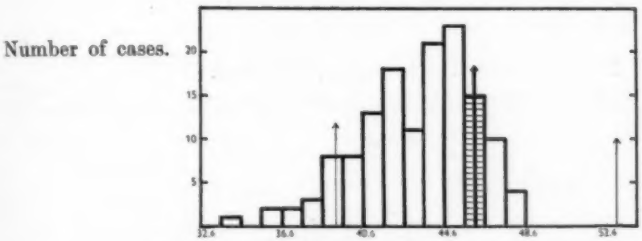
Radius 5. Pineal body—fossae occip.

The normal series, 200 cases.



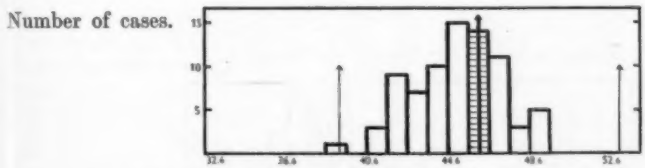
Radius 5 as percentage of the length of the cranium.

Tumours above the tentorium, 139 cases.



Radius 5 as percentage of the length of the cranium.

Tumours below the tentorium, 78 cases.

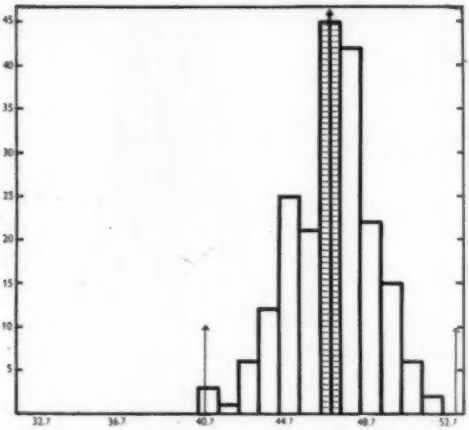


Radius 5 as percentage of the length of the cranium.

Radius 6. Pineal body—opisthion.

The normal series, 200 cases.

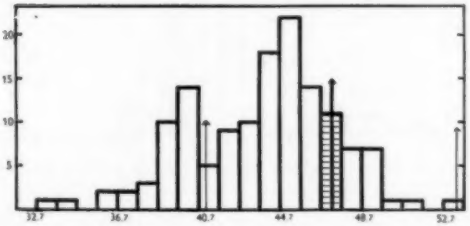
Number of cases.



Radius 6 as percentage of the height of the cranium.

Tumours above the tentorium, 139 cases.

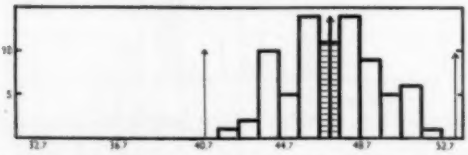
Number of cases.



Radius 6 as percentage of the height of the cranium.

Tumours below the tentorium, 78 cases.

Number of cases.



Radius 6 as percentage of the height of the cranium.

A study of the graphs shows partly that the normal material has a normal distribution and partly that there is also a very marked difference between both groups of supra- and infratentorial tumours. In cases of tumours above the tentorium there is an oblique grouping of the observations in such a manner that an over-representation of plus values, *i. e.* values that are greater than the average in the normal series, exists for the front and upper radii (2 and 4) whilst the back and lower radii (5 and 6) show an over-representation of minus values. But the plus values for the front and upper radii and the minus values for the back and lower radii indicate that a displacement of the pineal body has taken place in a backward and downward direction. On the other hand, in cases of infratentorial tumours the distribution is more even and more in conformity with a normal distribution.

As a matter of fact a displacement of the pineal body has occurred in a backward and downward direction in 50 % of the cases with tumours above the tentorium with a probability of at least 1/80. On the other hand in the group with infratentorial tumours only 11 cases (14 %) presented similar values, the majority of which (except 2 cases) in a backward and downward direction. A displacement of the pineal body backwards and downwards is therefore rare in cases of infratentorial tumours so such a displacement is of a certain importance in distinguishing between a tumour situated above and one situated below the tentorium.

Localization	Number of cases	Within $M \pm \sigma$	Outside $M \pm \sigma$ Probabil. 1 : 3	Outside $M \pm 1.5\sigma$ Probabil. 1 : 7	Outside $M \pm 2\sigma$ Probabil. 1 : 22	Outside $M + 2.5\sigma$ Probabil. 1 : 80	Outside $M \pm 3\sigma$ Probabil. 1 : 370	Lateral displacement at least 3 mm
Meningiomas	43	2	41	37	31	27	19	10
Tumours of frontal lobe	22	1	21	19	14	12	9	6
Tumours of motor region	5	—	5	5	5	4	4	—
Tumours of parietal and occipital lobes	8	1	7	4	4	4	2	—
Tumours of temporal lobe	19	—	19	15	7	3	2	2
Tumours of hypophysis.	27	4	23	16	9	5	3	—
Tumours of basal ganglia	15	—	15	15	15	14	11	—
Tumours of cerebellum.	43	1	42	33	17	7	1	—
Acoustic tumours	35	2	33	23	9	4	1	—
Total	217	11	206	167	111	80	52	18

Fig. 7. The material showing cases in the different groups brought together in statistical classes according to the measurement which most deviates from the mean.

Fig. 7 gives a more detailed survey of the tumours in the material. The position of the pineal body is indicated according to the measurement which deviates most from the normal value.

By way of example, there are 43 cases of meningioma in the material (see fig. 7) of which 27 present a position of the pineal body such as can appear normally only in 1 case out of 80 thus indicating a displacement of the brain substance. If, moreover, several measurements from the pineal body also have abnormal values which is usually the case, the probability of dislocation increases further. If the measurements have finally undergone such changes which usually take place in displacement of the brain substance, *i. e.* large measurements forwards and upwards and small ones backwards and downwards, it increases the probability of an expansive process within the cranium to such a degree that it can scarcely be neglected.

It will also be seen from fig. 7 that a displacement of the pineal body laterally has occurred in 18 cases of supratentorial tumours but not at all in any of the cases with tumours beneath the tentorium. The displacement has always taken place in the direction to the healthy side. Only in those cases where a lateral displacement of at least 3 mm is present can it be regarded as being really established. In this material the extent of the displacement varies from 3 mm to 15 mm.

With the development of an expansive process above the tentorium, the central parts of the brain are displaced backwards and downwards through the incisura tentorii towards the posterior cranial fossa. The measurements of the radii are diverging, now in the longitudinal direction of the cranium, now in the vertical direction, without this difference allowing of definite conclusions regarding the position of the tumour. As a rule, however, the downward displacement is predominant, presenting changes of the measurements in the vertical direction.

The supratentorial tumours that lie in front of the pineal body — for instance, in the frontal lobe and basal ganglia — often cause a more pronounced displacement in a backward and downward direction than the tumours which lie more laterally to the pineal body as, for instance, in the temporal lobe.

The question of the significance of hydrocephalus for the position of the pineal body has not yet been solved. The widening of the ventricular system probably plays a part in the displacement of the pineal body, but it can hardly be a matter of fundamental importance, judging by the observation of the pineal body in the cases of tumour in the posterior cranial fossa, where the hydrocephalic condition is as a rule well marked, whereas the displacement of the pineal body is rare.

Displacement of the pineal body may also be affected by pathological conditions other than tumours. The condition for displacement should be present in every expansive process which develops within the cranium.

There is, accordingly, not the slightest doubt that a displacement of the pineal body should be regarded as an important sign of tumour.

especially as a displacement of the pineal body is often the only roentgenological sign of tumour which can be shown in an ordinary examination. Through examinations made during recent years of the displacement of brain substance the position of the pineal body has aroused renewed interest and gained an importance beyond the indicating of an expansive process which can be made with greater accuracy by ventriculography and arteriography. For the understanding of the clinical tumour pictures with varying remote symptoms from the parts of the brain which are not exposed to direct infiltration by the tumour, one can no longer disregard the importance of the changes in shape of the brain substance. These changes in shape can cause serious symptoms such as cramps, paralysis etc. and can bring about threatening acute conditions with more calamitous consequences for the patient than the position of the tumour itself can cause. A proved, more or less considerable change in the position of the pineal body can here be taken as a warning. It is possible to follow the postero-inferior displacement of the brain substance with filling out of the basal subarachnoidal cisterns by observing the position of the pineal body. The calcification of the pineal body is situated in front of and above these basal cisterns, right in front of the entrance to the incisura tentorii and therefore has every possibility of marking a displacement of the central parts of the brain in a sagittal as well as in a frontal plane. If one were to place an indicator in the brain in order to study the displacement of the brain substance, one would hardly be able to find a more suitable place for the purpose than in the pineal body. *Quite simply one can regard a postero-inferior displacement of the pineal body as a sign of the presence of a tentorial pressure cone.* For this reason the determination of the position of the pineal body must be an integral part of the examination of suspect expansive process in the same way that, for instance, the eyes are examined.

SUMMARY

The work intends to give a brief survey of our knowledge about the displacement of the brain substance in expansive intracranial processes and to compare the pathoanatomical, clinical and experimental observations met with in literature with similar observations concerning this displacement published by the author in 1939, as demonstrated by the displacement of the calcified pineal body during roentgen examination.

A displacement of the brain substance and the pineal body can occur, partly laterally and partly postero-inferiorally with a filling out of the great basal cisterns. In this way changes are brought about which go under the name of cerebellar pressure cone and temporal or tentorial pressure cone. A postero-inferior displacement of the pineal body can be regarded as a sign of the presence of a tentorial pressure cone. It occurs frequently in supratentorial expansive processes and can cause symptoms from the brain stem, the pyramidal tracts and the vessels in this region.

The method of determining the position of the pineal body given in the author's

previous work has here been simplified to be more useable in daily practice. Six radii are measured from the pineal body and are put in percentual relation to the length and height of the cranium. The statistically calculated probability for displacement of the pineal body can be read directly from a diagram for each radius. (Fig. 6.) Such a displacement of the pineal body should be regarded as being an important sign of displacement and change in shape of the brain substance.

ZUSAMMENFASSUNG

Die Arbeit bezweckt, eine kurze Übersicht unserer Kenntnis von der Verdrängung der Gehirnsubstanz bei expansiven, intrakranialen Prozessen zu geben und die im Schrifttum vorliegenden pathologisch-anatomischen, klinischen und experimentellen Beobachtungen mit ähnlichen Beobachtungen über diese Verdrängung zu vergleichen, die von Verf. im Jahre 1939 durch die Verlagerung der verkalkten Zirbeldrüse bei der Röntgenuntersuchung veranschaulicht wurden.

Eine Verlagerung der Gehirnsubstanz und der Zirbeldrüse kann teils seitlich und teils nach hinten-unten zu stattfinden mit Ausfüllung der grossen basalen Zisternen. Hierdurch entstehen Veränderungen, die zerebelläre Druck-konus und temporale oder tentoriale Druck-konus genannt werden. Eine Verlagerung der Zirbeldrüse nach hinten-unten kann als ein Zeichen einer tentorialen Druck-konus betrachtet werden. Dies kommt häufig bei expansiven Prozessen oberhalb des Zeltes vor und kann Symptome seitens des Gehirnstammes, der Pyramidenbahnen und der Gefässe dieser Gegend geben.

Die in der früheren Arbeit des Verfassers gebrachte Methode zur Bestimmung der Lage der Zirbeldrüse ist hier vereinfacht worden, um in der täglichen Arbeit besser verwendbar zu werden. Es werden sechs von der Zirbeldrüse ausgehende Radien gemessen und zu der Länge und Höhe des Schädels in prozentuale Beziehung gebracht. Die statistisch berechnete Wahrscheinlichkeit einer Verlagerung der Zirbeldrüse kann direkt an einem Diagramm für jeden Radius (Fig. 6) abgelesen werden. Solch eine Verlagerung der Zirbeldrüse ist als ein wichtiges Anzeichen einer Verdrängung und Gestaltveränderung der Gehirnsubstanz anzusehen.

RÉSUMÉ

Le travail vise à donner un bref aperçu de nos connaissances sur les déplacements de la substance cérébrale dans les processus intracraniens expansifs, et à comparer les observations anatomo-pathologiques, cliniques et expérimentales rencontrées dans la littérature, aux observations semblables concernant ces déplacements que l'auteur a publiées en 1939, où ces derniers étaient démontrés par les changements de position de la glande pinéale calcifiée, à l'examen radiologique.

Un déplacement de la substance cérébrale ainsi que de la glande pinéale peut se produire, en partie latéralement et en partie en direction postéro-inférieure, lors du remplissage des grandes cisternes basales. De cette façon surviennent des changements appelées communément cône de pression cérébelleux ou cône de pression temporal ou tentoriel. Un déplacement postéro-inférieur de la glande pinéale peut être considéré comme un signe de la présence d'un cône de pression tentoriel. Cela arrive fréquemment dans les processus expansifs supra-tentoriels et peut donner lieu à des symptômes du côté du tronc cérébral, des voies pyramidales, et des vaisseaux de cette région.

La méthode, indiquée dans le travail précédent de l'auteur, pour déterminer la position de la glande pinéale a été, ici, simplifiée afin de la rendre mieux utilisable dans la pratique journalière. Six rayons sont mesurés à partir de la grande pinéale et l'on établit leur rapport en pour-cent avec la longueur et la hauteur du crâne. La probabilité

calculée statistiquement, d'un déplacement de la glande pinéale ressort directement d'un diagramme pour chaque rayon (Fig. 6). Pareil déplacement de la glande pinéale peut être considéré comme un signe important de déplacement et de changement de forme de la substance cérébrale.

LITERATURE

Allison, R. and Morrison: J. of Neurol. and Psychiatry 4. 1941.
Antoni, N.: Acta med. scand. 109, 1941.
van Gehuchten, P.: L'encéphale 2, 1937.
Groenevald, A. and Schaltenbrand, G.: Deutsch. Zschr. f. Nervenheilkunde 97, 1927.
Hasenjäger, T. and Spatz, H.: Arch. f. Psychiatrie 107, 1938.
Jefferson, G.: Arch. of Neurol. and Psychiatry 40, 1938.
Kernohan, J. and Woltman, H.: Arch. of Neurol. and Psychiatry 21, 1929.
Lilja, B.: Acta Radiologica 1939. Suppl. 37.
Lysholm, E.: Das Ventrikulogramm, Stockholm 1935 and 1937.
Meyer, A.: Arch. of Neurol. and Psychiatry 4, 1920.
Moore, M. and Stern, K.: Brain 61, 1938.
Perret, G.: Zentralblatt f. Neurochirurgie 5, 1940.
Quincke, H.: Deutsche Klinik 6, 1906.
Reichardt, M.: Allg. Zschr. f. Psych. 75, 1919.
Riessner, D. and Zülch, K. J.: Deutsche Zschr. f. Chirurgie 253, 1940.
Scheinker, M.: Arch. of Neurol. and Psychiatry 53, 1945.
Schüller, A.: Spez. Path. u. Ther. Suppl. 3—5, 1912.
Schwarz, G. and Rosner, A.: Arch. of Neurol. and Psychiatry 46, 1941.
Smyth, G. and Henderson, W.: Journal of Neurol. and Psychiatry 1, 1938.
Spatz, H. and Stroescu: Der Nervenarzt 1934.
Tönnis, W.: Zschr. f. die gesamte Neurologie und Psychiatrie 161, 1938.
—, Arch. f. klin. Chir. 193, 1938.
Vastine, J. H. and Kinney, K.: Amer. Journ. Roentgenol. 17, 1927.
Vincent, C., David, M., and Thiébaut, F.: Revue neurologique 65, 1936.
Winkelbauer, A.: Arch. f. klin. Chirurgie 150, 1928.

FROM THE ROENTGENOLOGICAL DEPARTMENT OF THE UNIVERSITY HOSPITAL OF OSLO, NORWAY (CHIEF: PROFESSOR TORLEIF DALE, M. D.)

ABOUT THE ANGIOGRAPHIC VISUALIZATION OF THE POSTERIOR CEREBRAL ARTERY, ESPECIALLY BY INTRACAROTID INJECTION OF CONTRAST[1]

by

Arne Engeset

Moniz has found in his angiographic material that the posterior cerebral artery could be seen on one side in more than 20 per cent of his carotid angiograms, and in 3 per cent bilaterally.

Barahona Fernandes found a higher percentage in oligophrenia, more than 32 per cent on one side. This was interpreted as a sign of a lower morphogenetic development in such patients. Moniz points out, according to the works of various authors (Hindze, Rabinowitch and Sacharowa) that the posterior communicating artery in the lower forms of monkeys is of almost the same caliber as that of the posterior cerebral artery. In the more highly developed apes, however, as for example in the gorilla, that very artery is thin as generally the case in *homo sapiens*.

Moniz is of the opinion that the arterial pressure in the basilar trunk is a little lower than the intracarotid pressure. When the posterior communicating artery meets the posterior cerebral artery the increased thinning of the contrast will not usually interfere with the visualization of that vessel.

Other investigators — Löhr, Fisher and Shimidzu — suggest the possibility of a collateral circulation from the carotid artery to the posterior cerebral artery in cases of internal hydrocephalus, tumours in the basal ganglia, and in some cases of tumours in the acoustic nerve.

The opposite possibility, that the blood-stream should pass from the basilar trunk to the carotid vascular area, is disputed by Moniz. Some cases, however, especially of carotid thrombosis (Krieg, Engeset, Frøvig) show angiographically a very probable collateral circulation in

[1] Read at the Congress of The Northern Neurosurgeons at Oslo, September 1947; submitted for publication, March 15, 1948.

this direction also. Patients are known to live after bilateral thrombosis in the carotid arteries.

From the technique in carotid angiography we know that we can obtain bilateral contrast-filling of the intracranial carotid branches by injecting contrast into the one carotid artery simultaneously with manual compression of the other. Analogous technical procedures to get filling of the posterior cerebral artery, are not yet known.

We know that bilateral ligation of the carotid artery has been performed, and that the patient has survived such procedure. This must be due wholly, or in part, to collateral circulation from the basilar trunk to the carotid vascular area, in the same manner as in carotid thrombosis.

Theoretically it would seem likely that bilateral compression of the *vertebral artery* would force the blood-stream from the carotid syphons to the basilar trunk. DANDY has arrested the blood-flow bilaterally in one case, and the patient died suddenly. He points out, however, that ALEXANDER in 1882 ligated both vertebral arteries with success at the same operation. DANDY seems to be of the opinion, therefore, that the grave arteriosclerotic changes in the intracranial vessels was the deciding factor in this case.

Many of these problems should certainly be studied *in vivo*, and there is some reason to believe that with a more specialized angiographical technique some of them might be solved.

MONIZ points out, rightly, that it may be more difficult to see the posterior cerebral artery by vertebral angiography, because it is filled bilaterally. At the same time cerebellar vessels also may be seen in such great quantity that it may be impossible to differentiate the individual vessels and their branches from each other. (Fig. 2.)

The lateral view in the usual carotid angiography shows that the posterior cerebral artery — when it is visualized — comes from the carotid syphon. In some cases the first part (the posterior communicating artery) is thin. From the junction of the posterior communicating artery and the posterior cerebral artery the latter proceeds backwards with a distinctly greater caliber to a bifurcation projected over the temporal bone. This bifurcation is usually characteristic of that artery. FOIX and MASSON, and others, describe a *tri*furcation of the posterior cerebral artery. The »ramus anterior» which goes to the lower anterior surface of the temporal lobe, is disputed by MONIZ. It may be seen, nevertheless, in some of our angiograms. The two branches of the bifurcation end in the temporo-occipital region. The upper medial branch reaches the cuneus.

From the posterior cerebral artery some branches pass to the posterior part of the thalamus and the infrathalamic region. The posterior chorioidal artery reaches the plexus chorioideus of the third ventricle

Fig. 1. Percutaneous angiography (normal angiogram). Bilateral contrast-filling by manual compression of the contralateral carotid artery.

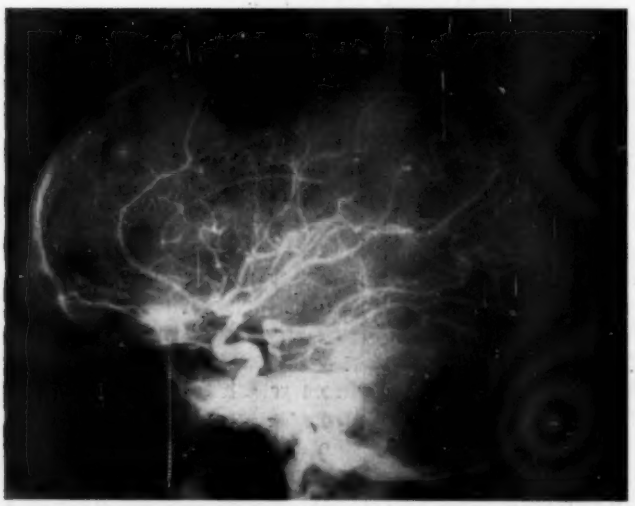


Fig. 2. Bilateral contrast-filling of the posterior cerebral arteries and the basilar trunk (usual injection in one carotid artery).

and the upper part of the lateral ventricles. A small branch reaches the hippocampus also.

In short, we see that the posterior cerebral artery supplies the lower surface of the temporal and the occipital lobes and the cuneus. It also supplies more than half of the optic thalamus and partly the cerebral peduncles. FOIX and MASSON tried to construct a clinical »syndrome de l'artère cérébrale postérieure», where alexia was the prominent symptom. I would suggest that a more specialized angiographical technique in combination with a special clinical study might be important in this respect.

By reading the works of MONIZ, LYSHOLM, OLIVECRONA, RIECHERT, LÖHR, and the Text-Book of X-ray Diagnosis by British Authors, I have got the impression that these investigators all still have much work to do, as we ourselves also have. I will try a small attack, therefore, with such material as we have, in the hope that others with better results will supplement ours.

In this preliminary study I have perused angiograms from 438 patients. The posterior cerebral artery was visible in 23.5 per cent (in 103 patients). In 250 patients from the Neurological Department the percentage was found to be 14.8. In 188 patients from the Neurosurgical Section a percentage of 35.11 was registered. This curious difference may have various causes. The material from the Neurosurgical Section mostly represents patients with organic brain diseases, 114 with intracranial tumours, 8 cases of aneurysms, and so forth. The possibility of a morphogenetic lower order of development similar to the findings of FERNANDES in oligophrenia, must be taken into consideration. The abnormal intracranial pressure in many of these patients, combined with atypical circulation in the circle of Willis, may be a deciding factor. But the technical procedure in the angiographic examination also may be of some importance. Most of the patients in this period from the Neurological Department have been angiographed by the percutaneous technique, whilst most of the patients from the Neurosurgical Section have been angiographed after exposure of the carotid arteries. Further investigations may solve some of these problems.

While in many lateral pictures the posterior cerebral artery could be demonstrated beautifully, it was difficult to discern in the frontal pictures. In some cases where the direction of the rays had been parallel to a line through the supraorbital arch and the external acoustic meatus, the artery was better visualized. In the frontal picture the supraorbital arch was projected over the superior border of the petrosal bone, and the carotid syphon as also the posterior cerebral artery were outlined clearly. In most of our earlier pictures the carotid syphon is projected behind the dense bony structures of the anterior cavity of the

skull. In this latter projection we may see the carotid syphon and its branches M 1 and A 1, and we may judge their anatomical position. With the tube tilted a little cranially, however, we may judge these structures as well, and we get a better view of the posterior cerebral artery also.

OLIVECRONA and SJÖQVIST have shown a picture with dislocation of the basilar artery in the usual frontal projection which has been performed by a vertebral angiography, however. In carotid angiography the contrast-filling of the posterior cerebral artery is seldom combined with visualization of the basilar artery. We have tried also a 35 degrees tilting of the tube cranially. This projection we have used successfully in the usual percutaneous carotid angiography. We must then inject 8 cc. uriodone once for this exposure. Medial or lateral dislocation probably is best seen in this projection. An axial view in vertebral angiography, as advocated by HODGES and LIST, has been employed in some cases, but we do not like it because the irregular bony structures of the base of the skull do not constitute a fitting background for the arteriograms.

I have selected 50 cases in our material for study of the angiographical anatomy, 35 of which were made in two planes and three bilaterally. A selected normal material was not available, but still some cases give hints of value.

Lateral view

Usually we see that the *posterior communicating artery* forms a small arch between the carotid syphon and a small point which corresponds to the anterior part of the posterior cerebral artery. This arch is basally convex, and the length was found to average 1.11 cm. in 47 patients, varying between 2 and 0.4 cm. (see fig. 3). In cases of occipital tumours it was in one case 1 cm., in another case 0.4 cm. In the latter case the arch had the appearance as if it was compressed from behind with a resultant angular point downwards (fig. 4). Perhaps this deformity could be found also in other cases of occipital tumours. Frequently the caliber of the posterior communicating artery may be seen to be smaller than that of the posterior cerebral artery. As a direct continuation of the posterior communicating artery we see the main trunk of the posterior cerebral artery which ends usually in the bifurcation described by MONIZ as characteristic of that artery. Usually this part of the artery also is basally convex. The average length in 47 patients was 2.54 cm. with a variation between 1.6 and 3.5 cm. In some cases it was difficult to locate the exact beginning of the bifurcation. In some cases a probable ramus anterior could be found in the usual distance from the syphon, while a

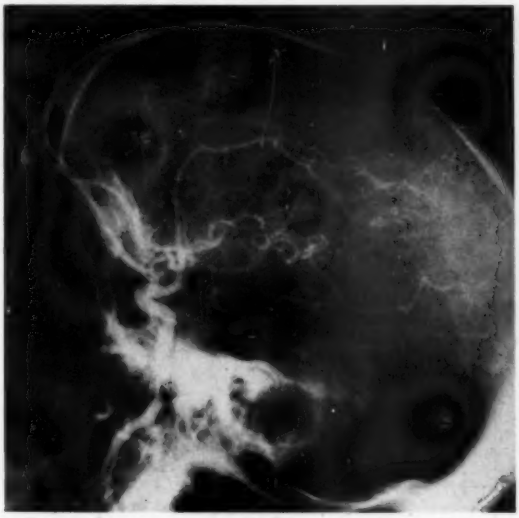


Fig. 3. A case of multiple small cancer metastases.
The beginning of the posterior communicating artery. ⟶
The foremost part of the posterior cerebral artery (perhaps the end of the basilar artery). ⟷
The bifurcation of the posterior cerebral artery. ⟷

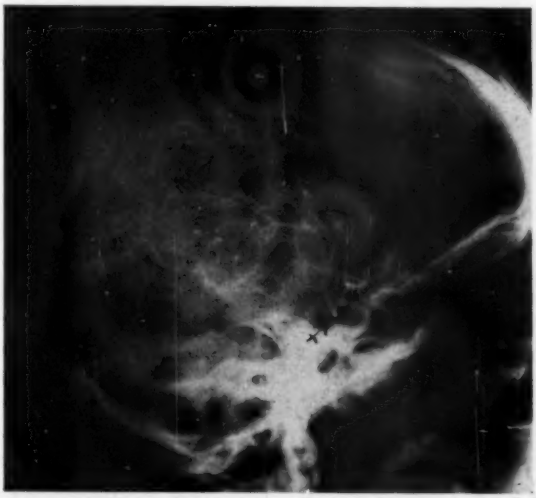


Fig. 4. A case of occipital glioblastoma multiforme.
The distance between the beginning and the end of the posterior communicating artery is reduced to 0.4 cm. ⟷
Angular point downwards. ⟷

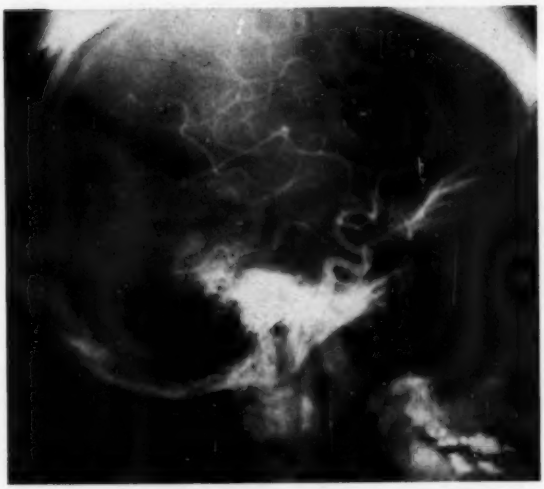


Fig. 5. A case of occipital glioma (also some parietal extension).
Abnormal elevation of the first part of the posterior cerebral artery. ⟶
Angular point downwards of the posterior communicating artery, as seen also in fig. 4. ⟷

Fig. 6. Deep-seated parietal glioma.
Arrow on a slightly upward-directed point near the bifurcation of the posterior cerebral artery (caused by a tentorial impression?).

bifurcation in such cases could be seen further backwards. In cases with occipital tumours we found the length of this part of the artery to vary between 2.4 and 2.8 cm., which seems to be quite normal. In another case of occipital tumour we see the same angle as mentioned before in occipital tumours of the posterior communicating artery. Behind this artery we see a very atypical arcuate elevation of the first part of the posterior cerebral artery which surely corresponds to a direct forward pressure of the tumour (fig. 5). A pathological circulation is distinctly supplied here from the posterior cerebral arteries and gives the type diagnosis. We shall study some pathological cases.

In a case of parietal deep-seated tumour we found another small change, a small angular point just in front of the bifurcation (fig. 6). In a case of intracranial tumour, which came for autopsy, with a distinct furrow in the temporal lobe on account of an impression from the tentorial ridge, it could be clearly seen that this impression also affected the posterior cerebral artery near the bifurcation. I am sorry to say that we had no angiograms of that patient, but I think that this small angular deformity may arise from the same cause. It should be verified, however.

In four of 438 cases we have seen contrast-filling also of the upper part of the basilar artery. In these cases 16 cc. contrast has been injected in the common carotid artery by the method of MONIZ. To get this retrograde filling via the subclavian artery to the vertebrals, it is probably best to use such technique. With percutaneous technique we have compressed the injected artery peripherally to the puncture by manual compression to get a retrograde filling of the vessels in the posterior cavity of the skull. This technique has not yet proved completely successful, but we have hopes for the future. The method described by TAKAHASHI and later by WICKBOM (discussion on this paper at the Congress of Northern Neurosurgeons at Oslo, 1947) of injecting the vertebral artery percutaneously, has been no success yet in our hands.

Frontal view

The shape and visualization of the posterior cerebral artery in the frontal projection is not mentioned in the literature, to my knowledge. LIST and HODGES have a drawing in which the artery can be seen. We have a case with angiographical and encephalographical normal findings which may be discussed as probably normal, where the posterior cerebral artery is very ideally seen (fig. 7), partly also because the anterior cerebral artery is not filled with contrast. We do not need to take into account, therefore, a differentiation of branches from this vessel, which may be difficult in some cases.

Fig. 7. Normal angiogram. The anterior cerebral artery not filled with contrast (technical variation).

The posterior communicating artery. ⟨ The posterior cerebral artery. ⟶

The bifurcation. (Roentgen tube tilted about 15 degrees cranially.) ⟷

The syphon and the posterior cerebral artery is projceted free from the bony structures of the orbit and the anterior cavity of the skull.

We see that the posterior communicating artery proceeds medially. From the probable termination of that artery we see the posterior cerebral artery as a laterally convex bow which ends in a typical bifurcation, and which surrounds the brain stem. The upper branch of the bifurcation is medially convex in its first part, but spreads more peripherally backwards near the midline. The lateral branch of the bifurcation is also medially convex, spreading later in the area between the former branch and the sylvian group. A small ramus anterior may be seen in both planes.

Based on other cases we have arrived at the opinion that this shape of the artery is relatively constant. Where the anterior cerebral artery has branches crossing the branches of the posterior cerebral artery, the best identification is, also in the frontal projection, the figure of the bifurcation which may be seen in most cases. If there is doubt as to the distribution of the posterior cerebral artery or its branches a new picture with 35 degrees tilting of the tube cranially is advised (fig. 8). Such a procedure involves a technique by which the needle is not removed before the pictures have been inspected in the dark room. According to

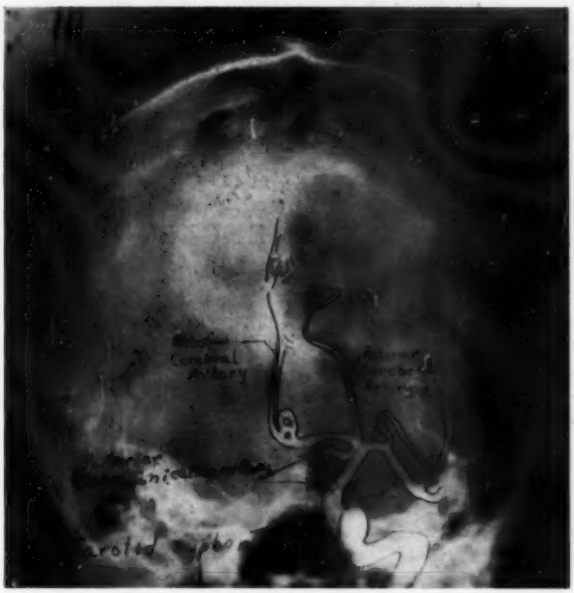


Fig. 8. Arteriogram in the half-axial view. Main vessels drawn up to show the anatomical relationship.

The communicating posterior artery. ⟨

The carotid syphon. ⟶

such a preliminary evaluation in the dark room special new exposures may be made, which then may be decisive.

SUMMARY

Some facts and problems in connexion with the angiographic visualization of the posterior cerebral artery, have been discussed. A special frontal projection with a tilting of the tube about 10 degrees cranially is advocated as a routine. For special cases it is advised to take angiograms in the half-axial projection also.

ZUSAMMENFASSUNG

Gewisse, mit der angiographischen Darstellung der Arteria cerebralis posterior zusammenhängende Tatsachen und Probleme werden besprochen. Als Routinemethode wird eine besondere Frontalprojektion mit Neigung der Röhre etwa 10° kranialwärts empfohlen. In besonderen Fällen wird angeraten, auch in der halb-axialen Projektion Angiogramme aufzunehmen.

RÉSUMÉ

Discussion de certains faits et problèmes en relation avec la mise en évidence, par angiographie, de l'artère cérébrale postérieure.

L'auteur plaide en faveur d'une projection frontale spéciale, avec inclinaison de l'ampoule d'environ 10 degrés du côté proximal, comme méthode ordinaire. Dans des cas particuliers il recommande d'exécuter aussi les angiogrammes en projection demi-axiale.

REFERENCES

Dandy, W.: Intracranial Arterial Aneurysms. New York, 1945.

Fernandes, Barahona and Alves, Abel: A angiografia cerebral nos oligofrénicos. Arqu. de Med. Legal. Lissabon 8 (1939).

Fischer, Erich: Die Arteriographische Diagnostik der Stirnhirn und oralen Stammgangliengeschwülste. Zbl. f. neurochir. 4, 72, 1939.

Foix, Ch. and A. Masson: Le Syndrome de l'artère cérébrale postérieure. Presse médicale. 32, 361, 1923.

Frovig, A.: Bilateral Obliteration of the Common Carotid Artery. Acta Psych. et Neur. Suppl.: XXXIX, Copenhagen, 1946.

Krieg, W.: Kollateralkreislaufentwicklung bei Durchblutungsstörungen des Gehirns in arteriographischen Bild. Zbl. f. Chir. 11, 562, 1939.

List, C., F. and Fred J. Hodges: Angiographic Diagnosis of Intracranial Lesions by vascular Displacement. Radiology 47, 319, 1946.

Lysholm, E.: Die Arteriographie. (Neue Deutsche Chirurgie, Band, 50.) Specielle Chirurgie der Gehirnkrankheiten 111 Band, p. 159. Stuttgart 1940.

Löhr, W.: Die Arteriographie der Gehirngefässe. Neue Deutsche Klin. Ergänzungsband. 1936.

—, Kreislaufstörungen im Gehirn, bedingt durch Gefässkrankheiten und raumbeengende Prozesse in arteriographischer Darstellung. Fortschritte a. d. G. d. Roentgenstrahlen, 59, 474, 1939.

Moniz, Egaz: Die Cerebrale Arteriographie und Phlebographie. Handbuch der Neurologie. Ergänzungsserie 2. Berlin 1940.

Olivecrona, H.: Die Arteriographie. Neue Deutsche Chirurgie, Band 50. Spezielle Chirurgie der Gehirnkrankheiten. 111 Band. p. 159. Stuttgart 1940.

Riechert, T.: Die Arteriographie der Gehirngefässe. Berlin 1943.

Shanks, Kerley and Twining: A Text-book of X-ray Diagnosis by British Authors. London 1938.

Shimidzu, K.: Beiträge zur Arteriographie des Gehirns, einfache percutane Metode. Archiv für klin. Chirurgie. CXXXVIII, 205, 1937.

FROM THE ROENTGEN DEPARTMENT OF OSLO MUNICIPAL HOSPITAL, ULLEVÅL, NORWAY
(CHIEF: J. FRIMANN-DAHL, M. D.)

HEMATOMA OF THE JEJUNUM WITH SUBILEUS[1]

by

Kjell Liverud

One of the most rarely seen causes of ileus is the simple hematoma in the intestinal wall, which must be distinguished from the hemorrhagic infiltration seen in case of circulatory derangements of the blood supply to the intestine. The hematoma is in most cases subserously or submucously situated, and if it is sufficiently large it may, either by filling up the lumen of the bowel or by producing invagination, give rise to intestinal obstruction or even to fully developed ileus.

In the literature we find few accounts of this condition, which is most often seen where there is increased tendency to bleeding, as in hemophilia (KHANTZ 1908) or in hemorrhagic purpura (SUTHERLAND 1904, GAMSTED 1933). The condition is, however, not necessarily due to increased tendency to hemorrhage. VOGEL in 1914 reports the finding of a hematoma the size of a fist in the sigmoideum of a patient who had some days previously undergone an operation for inguinal hernia under local anesthesia, and he believes the bleeding from the intestinal wall to have been due to injury by the needle used for injecting the anesthetic.

LAMY and FONT-RÉAULX in 1937 describe a similar case, where the lesion is supposed to have occurred during intraperitoneal infusion of saline solution. The case reported by LARGHERO and IBARZ (1936) must be regarded as traumatic, since it arose after reposition of an incarcerated hernia. BRAUN and WORTMANN (1924) found a hematoma about 20 cm. long in the ileum of a patient with a mesenteric cyst and they suppose that the hematoma was due to a trauma caused by compression of the bowel between the spinal column and the cyst, but no such trauma was found to have existed.

The cause of the ileus condition — the hematoma — has been found as a surprising discovery on operation or on post-mortem examination.

[1] Submitted for publication, May 12, 1948.

In the literature accessible to me I have not found any roentgenological description of the condition and I shall therefore give an account of the following case:

On Feb. 21st 1946 a three-year-old boy was admitted to Oslo Municipal Hospital, Medical Dept. VII, on the diagnosis: Cerebropathia. After a preliminary examination he was given an enema and was at once transferred to Surgical Dept. II of the same hospital on the diagnosis: Volvulus? When he was 10 months old he had lain in hospital some days for observation on account of a brief attack of diarrhea. When 15 months old he had had an operation for bilateral mastoiditis, with uncomplicated course. Otherwise he had been well until the present illness occurred.

As to this illness his parents could state that in the last two days he had constantly had attacks of vomiting. The vomit contained the food he had eaten and was partly bile-coloured, but it contained no blood. He had become increasing weak, tired and emaciated and suffered from thirst. The stools had been »scanty» and likewise the urine. No blood was observed in the stools.

The patient was pale, inert, somewhat apathetic and had dark rings around the eyes. He was free from fever. Pulse 140, regular. The tongue was dry and furred. He had a dried up appearance and was constantly asking for something to drink.

The abdomen was of ordinary shape and size, not distended. The abdominal wall was soft and no tumours or obstructions could be palpated. The usual clinical examinations otherwise gave negative results.

Hemoglobin: 108 per cent. (Subsequent examination showed normal duration of bleeding and coagulation.)

Thus the only information furnished was that the patient had had attacks of vomiting during two days and presented symptoms of desiccation, while the clinical findings were otherwise negative.

The patient was at once subjected to roentgenological examination in view of the diagnosis: Volvulus?

General pictures of the abdomen, taken in upright and in recumbent position with horizontal radiation, showed fluid-level in the stomach and duodenum, otherwise no gas in the intestine. As the patient had been given an enema a couple of hours before, no definite significance could be assigned to the airless state of the bowel, but it was believed that the possibility of volvulus could be excluded. On account of this element of uncertainty and the presence of fluid in stomach and duodenum an examination of the intestinal tract with contrast medium was recommended, in case of continued vomiting.

The patient was kept under observation and was given intravenous injections of from 1 to 1.3 litres of liquid per 24 hours. The attacks of vomiting continued. The general condition remained practically unchanged.

Five days later the patient was given a couple of tablespoonfuls of barium per os and the subsequent roentgen examination made the matter clear.

Fluoroscopy two hours after ingestion of the contrast meal showed a considerable distention of the duodenum, but no dilatation of the stomach. On slight compression of the horizontal part of the duodenum the contrast substance flowed through a narrow portion of the jejunum, about 10 cm. long, from the duodeno-jejunal flexure downwards. From this narrow part the contrast spread out in lateral direction along distended semicircular folds and embraced a nearly orange-sized tumour,

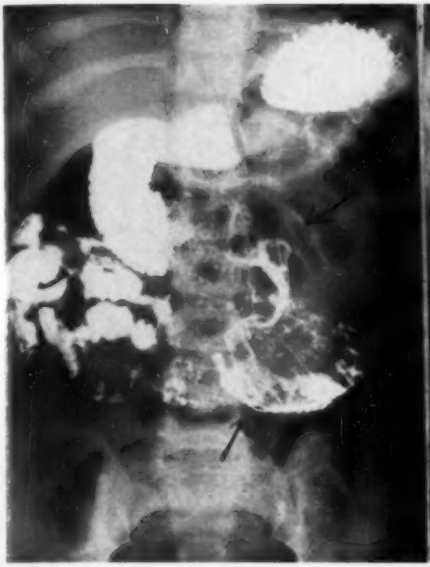


Fig. 1. Two hours after contrast meal. Dilatation of duodenum. Upper part of jejunum is narrowed. Tumour downwards and laterally.

Fig. 2. Three hours after contrast meal. Mucous membrane relief in the bowel which surrounds the lower part of the tumour.

which could be moved together with the contrastfilled portion of the bowel. The contrast substance surrounded the lower part of the tumour, which ended as a sharply defined bulb with even surface. It was not possible to get the contrast to spread over the upper, lateral part of the tumour, which was therefore supposed here to issue on a broad base from the wall of the intestine (Fig. 1).

On the picture taken after three hours the relief of the mucous membrane is distinctly seen in the distended bowel, and the contrast meal is passing through the narrow part (Fig. 2). After eight hours most of the contrast meal lies in the caecum. Some of it has been retained in the duodenum and jejunum. Some of the contrast lies smeared over the tumour, which is seen to have a smooth surface. The folds of mucous membrane in the distended bowel are seen both before and behind the tumour (Fig. 3).

After 24 hours practically the whole of the contrast meal lies in the colon. Only in the narrow part of the jejunum is there seen retention, with distinct mucous membrane relief also here. Medially is seen a niche-

Fig. 3. Eight hours after contrast meal. Surface of tumour smooth. Crossing of mucous membrane folds in the bowel which surrounds the tumour.

Fig. 4. Twenty-four hours after contrast meal. Retention of contrast in upper part of jejunum, with mucous membrane relief.

like projection, which is visible on all the photographs. Likewise in this part the mucous membrane is seen in distinct relief (Fig. 4).

Thus the roentgen examination revealed a relatively impeded passage in the upper part of the jejunum, as well as an almost orange-sized tumour, which could first be palpated during the screening and was found to be of soft, elastic consistence. It followed the movements of the intestine and was downwards enclosed by the distended bowel. The relief of the mucous membrane of the bowel ended upwards and laterally in a sharp »corner» (Figs. 2 and 3). There must here be assumed to have existed a tumour in the intestinal wall. Partly by blocking up the lumen, partly by reducing the peristalsis of the bowel, it produced a relative obstruction of passage, which led to the development of the clinical picture of high ileus. As the tumour had a smooth surface, with sharp delimitation downwards, and was of soft consistence, it was assumed to be a benign tumour, mostly suggestive of a lipoma, a cyst or adenomyoma.

The nichelike projection was a subject for many diagnostic speculations. The presence of an ulcer or of necrosis in a daughter tumour was precluded, partly on account of the distinct mucous membrane relief.

It could merely be established that there was here a projection clothed with mucous membrane in the narrow part of the jejunum.

The roentgenological diagnosis therefore was: Relative obstruction of passage in the upper part of the jejunum by a tumour, probably of benign nature: lipoma or cyst?

Operative treatment was clearly indicated and after preoperative administration of liquids there was done:

Laparotomia. Gastroenterostomia posterior. (Dr. KAAREM.)

The upper part of the jejunum for a length of 10 cm. was found to be blue-black in colour, with sharp delimitation from healthy intestine. The blue-black bowel was distended in spindle form and within it was felt a soft tumour nearly the size of an orange. When the surgeon tried to lift up the bowel the blackened serosa burst and a mass of black coagula and old blood flowed out. This was carefully wiped away. The bowel contracted and assumed an almost normal caliber. Through the ragged serosa one could see down to the muscularis, which was exposed to a large extent. It did not appear to be gangrenous, but for fear of subsequent cicatrisation there was made for safety's sake a posterior gastroenterostomy immediately below the diseased part of the bowel. The rest of the intestine and the abdominal cavity were inspected, but no other hemorrhages were found.

Thus there was here a subserous hematoma which had dislodged the serosa, stretched the muscularis and mucosa and forced both of them into the lumen of the bowel, as a tumour, and thereby produced difficulties of passage. Morphologically, the roentgen examination had in so far made the matter clear, and with information respecting trauma or an existing tendency to bleeding one might well have considered the possibility of a hematoma, a form of cyst. The nichelike projection may possibly be explained by assuming that the muscularis and mucosa at this place were perforated by a blood vessel which had resisted the pressure of the hematoma and had therefore drawn out the mucosa like the guy-rope of a tent.

The patient was re-examined some months later. He had been well since his discharge from hospital. Examination of the blood showed no signs of tendency to bleeding or hemophilia, of which there was likewise no history in the family. The patient's mother could now state that the lady who had brought the boy home when he got ill had seen him playing with some bigger boys, who had repeatedly kicked him violently in the stomach. The boy had fallen and could not rise. He cried and complained of pains. She carried him to his home, where he recovered, but two or three hours later he again got ill, had pains in the stomach and vomited. This had then continued for two days before a doctor was

called in. The traumatic cause of the hematoma should accordingly be extremely probable.

Besides giving an example of a rare cause of ileus the case shows the importance of roentgen examination in obscure abdominal lesions. In case of high ileus, where the typical signs of ileus, such as visible peristalsis and distention of the abdomen may be absent (ASSMANN), the examination by means of a contrast meal is of decisive significance for the diagnosis.

SUMMARY

A traumatic subserous hematoma of the jejunum, presenting the clinical signs of high ileus, is roentgenologically demonstrated.

ZUSAMMENFASSUNG

Ein traumatisches, subseröses Hämatom des Jejunum, das die klinischen Symptome eines hohen Ileus gab, wird röntgenologisch demonstriert.

RÉSUMÉ

Démonstration radiologique d'un hématome sous-séreux du jéjunum, présentant les signes cliniques d'un iléus de siège élevé.

REFERENCES

ASSMANN, H.: Die Klinische Röntgendiagnostik der Inneren Erkrankungen. Berlin. 1934.

BRAUN, W. & WORTMANN, W.: Der Darmverschluss. Berlin. 1924.

GAMSTED, E.: Acta Chir. Scand. 1933, vol. 73, p. 280.

KHANTZ, A.: Arch. f. Klin. Chir. 1908, vol. 78, p. 542.

LAMY, M. & DE FONT-RÉAULX, P.: Ann. d'anat. path. & d'anat. norm. med.-chir. 1937, vol. 14, p. 521.

LARGHERO, P. & IBARZ: Arch. urug. d'med. cir. y esp. 1936, vol. 9, p. 468 (cit.).

SUTHERLAND, G. A.: Brit. J. Dis. Child. 1904, vol. 1, p. 23.

FROM THE ROENTGEN DEPARTMENT OF OSLO MUNICIPAL HOSPITAL, ULLEVÅL, NORWAY
(CHIEF: J. FRIMANN-DAHL, M. D.)

ON THE ROENTGENOLOGIC PICTURE OF PULMONARY EDEMA[1]

by

Selmer Rennæs

Our knowledge of the roentgenologic picture of the acute as well as the chronic pulmonary edema is of a relatively recent date. Only for the last two decades reports have appeared in the literature.

The roentgenologic picture of pulmonary edema is described by several authors (COE & OTELL 1932, ZDANSKY, LELONG & BERNARD, ROESLER, ROUBIER, WERKENTHIN, KOMMERELL & WEDLER, NESSA & RIGLER, RENDICH, LEVY & COVE.)

The heart, as a rule, is enlarged as in the case of hypertension, and symmetrical, more or less confluent, perihilar ill defined patches of increased density are found. A striking feature is the central distribution of the opacities, leaving the apices, peripheral borders and bases relatively clear. Characteristically and as a contrast to the common picture of passive pulmonary congestion, the bronchies stand out clearly whereas the vascular markings are not seen. The changes may be transitory (ROESLER).

The chest roentgenogram alone is not conclusive. In some instances differentiation has to be made against any bilateral widespread opacities in the lungs, as bronchopneumonia or multiple hemorrhagic infiltration of pleura and lungs (DALE). As to the latter the opacities are scattered throughout the entire lung, also involving the peripheral areas.

Especially the differentiation between pulmonary edema and passive pulmonary congestion may give rise to diagnostic difficulties. However, both conditions when typical, present a characteristic picture. The passive pulmonary congestion is a passive vascular overfilling with associated perivascular and interstititial reaction. It is often associated with mitral heart. The hilar shadows are enlarged, the vessels stands out clearly in contrast to the bronchies which may be more or less effaced (compare the contrast to the pulmonary edema). In addition there may be fine miliary opacities causing a fluffy mothling in both lungs. Or there may be larger irregular shadows, ill defined and not very dense. The changes

[1] Submitted for publication, May 21, 1948.

are usually seen in basal parts, often associated with pleural exudate. In chronic cases fibrotic changes or calcifications may be scattered throughout the lungs.

The study of chest roentgenograms in the case of different forms associated with cardiac failure has elucidated the essential difference. Especially do American radiologists differentiate between edema an passive congestion. In some instances the edema may develop as a result of passive congestion although it may very well be found without signs of congestion being present.

With regard to the clinical picture and the clinical findings, the following cases present some interesting features:

Case 1. K. L. female, aged 84. For the last twenty years she had suffered from diabetes. Since 1933 a varying hypertension has been measured. 1933 RR 190/105, 1938 RR 160/90, 1941 RR 240/105, 1945 RR 220/120. In 1945 she was admitted to hospital on account of threatening diabetic coma. The patient was very thin, cyanotic, with slight edemas. The tongue was dry. The heart was enlarged, the apex beat being felt about 2 cm. laterally to the medioclavicular line. No murmurs could be heard over the heart. Crepitant râles could be heard in the right infrascapular region. Otherwise the clinical findings were essentially negative. Plenty of fluid was administered. The patient received 8,500 cc per os and 2,000 cc intravenously in the course of 4 days. During the same period the total diuresis was 2,500 cc, on one day 300 cc and no urine at all on another. The physical signs over the lungs remained unchanged. A chest roentgenogram (fig. 1) showed bilateral, mottled, ill defined areas of increased density in the upper parts of both lungs. The temperature was then 37.1° C.

The roentgenogram was interpreted as a bilateral bronchopneumonia. The patient died the next day. Postmortem showed some hypostasis, but edema in the central and upper parts of both lungs corresponding to the areas of increased density. No bronchopneumonic foci were found.

Case 2. O. H., male, aged 67. He has always been healthy. During the war the weight has fallen from 69 kg to 50 kg. For the last 14 days prior to the admission he has been troubled by abdominal pains and obstipation. An increasing distension of the abdomen had been noticed. He was admitted under the diagnosis: subileus, cancer coli? Physical examination showed an emaciated, dehydrated patient. The temperature was 36.8° C, the pulse 120, weak and could just be felt. It was difficult to measure the blood pressure, RR 80/40? No edema. The heart was not enlarged, and no murmurs were heard over the heart, no adventitious sounds over the lungs. In this case routine examination also included roentgenological examination. A chest roentgenogram (fig. 2) showed a mottled and ill defined area of increased density in the middle and lower zones of the lung, most marked on the right side. Roentgenological examination of the abdomen revealed meteorism and fluid in the peritoneal cavity. Shortly after the examination 1,800 cc of isotonic saline was administered intravenously. The patient's condition became gradually worse, and he died a couple of hours later.

Autopsy revealed cancer of the stomach, metastases and also cancer of the colon. The lungs were heavy and edematous. Microscopical examination showed a typical pulmonary edema. Otherwise no pathological changes were seen in the lungs. No bronchopneumonic foci or metastases that could explain the roentgenological picture were found.

Fig. 1.

Fig. 2.

Fig. 1. Roentgenogram taken the day before death showing mottled ill defined areas of increased density in both lungs. Postmortem: Pulmonary edema.

Fig. 2. Roentgenogram showing increased density in the middle and lower part of the lung. Postmortem: pulmonary edema.

Case 3. A. O., male, aged 53. During the last 5 months the patient had noticed that his vision had become impaired. The blood pressure had been high. On August 1st 1946, he was admitted to hospital on account of dyspnea. On the admission to hospital the temperature was 38° C., pulse 120, respiration 60, RR 240/180. The heart was enlarged, but no murmurs could be heard. Subcrepitant râles were heard over both lungs, most markly posteriorly. Chest roentgenograms were taken, pneumonia being suspected. The roentgen picture (fig. 3 A) revealed enlargement of the left ventricle, and ill defined opaque areas in the middle zones of both lungs. The peripheral parts were remarkly clear. The bronchial tree was faintly outlined, but the vascular markings were obscured by area of increased density. The patient was treated as a case of pulmonary edema, and some improvement was seen during the following days. This was also indicated by a control roentgenogram (fig. 3 B). Further clinical examination revealed nothing but the subcrepitant râles heard over the left lung. The dyspnea increased, but there was no frothy sputum. The patient died two days later. At autopsy an enlarged heart was found. The wall of the left ventricle was thickened, and the left auricle was somewhat dilated. The valves were normal. The lungs were heavy and firm. Microscopical examination showed thickening of the alveolar walls, some congestion, and fluid in the alveoli (pulmonary edema).

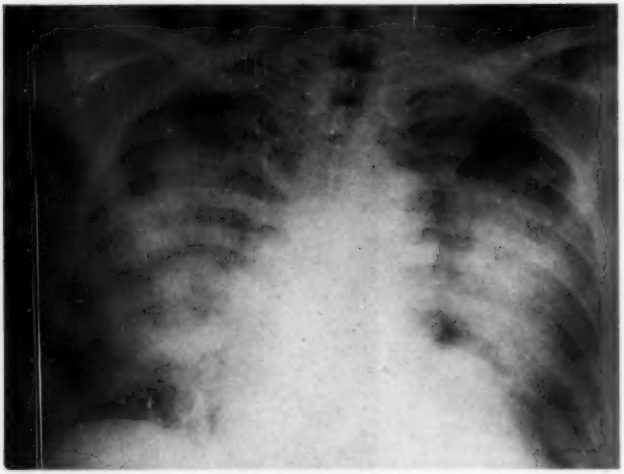


Fig. 3 A. Roentgenogram showing enlargement of the left ventricle, and ill defined opaque areas in the central part of both lungs. Translucent lung tissue in the periphery.

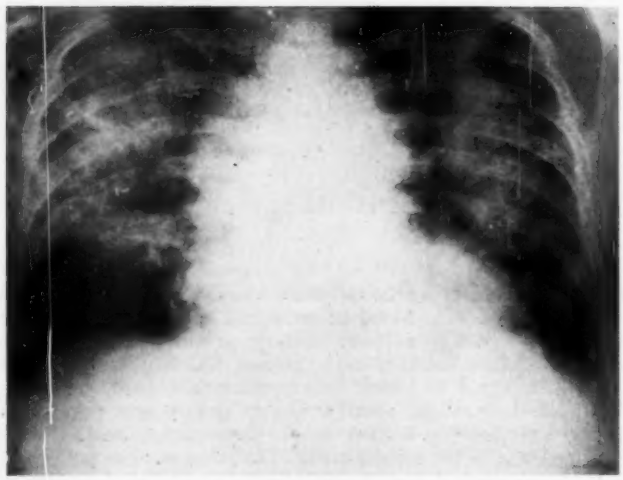


Fig. 3 B. Two days later after treatment. Opacities confined to the central part of the lung.

Comment

Autopsy was performed in all the 3 cases here reported, and the pathologico-anatomical examination verified the diagnosis of pulmonary edema. No other changes which might explain the roentgenological picture were found in any of the cases.

The production of edema *e. g.* in the subcutaneous tissue, depends on various factors, such as, the hydrostatic pressure in the blood vessels

and lymphatics, the osmotic pressure of the blood and tissue and the permeability of the capillary wall. Particularly should be noted the important part played by lymphatic obstruction. These factors we may call general factors. In the lung, however, some additional factors are involved.

Firstly, the lung contains air and has an abundant supply of blood vessels and lymphatics. Secondly, the lungs are enclosed in the pleural sac with its varying negative pressure. These particular factors have the following effect: The oxygenation of the alveolar wall depends entirely on the oxygen tension in the alveolar air as the vessels of the lung do not extend to the alveoli, but terminate in a capillary network around the bronchioli. In total bronchostenosis an equilibrium is rapidly established between the oxygen tension of the alveolar wall and that of the venous blood of the lesser circulation. DRINKER, by experiments, has shown that the alveolar cells are particularly sensitive to lack in oxygen. When there is an anoxemia of the pulmonary tissue, the permeability of the alveolar wall increases, thence there is a tendency to edema.

The capillary pressure in the subcutaneous tissue is 25—30 mm Hg whereas the pressure in the pulmonary capillaries is estimated to 10 mm Hg. For this reason the alveoli and bronchi are normally dry, fluid literally being forced into the capillaries. The negative pleural pressure does not at normal respiration when the pressure varies between — 5 and — 10 mm Hg, contribute to any demonstrable removal of fluid from pulmonary tissue. However, the forces respiration on effort (GRAHAM) or in relative bronchostenosis (DRINKER) as a result of which the pressure may fall to — 80 or — 90 mm Hg, may produce such a marked suction effect that exudate appears in the pleural cavity.

These particular conditions in the lung and the pleural cavity are of consequence to the roentgenological picture. The initial transudation of fluid takes place in the alveolar wall, later on also in the interstitial tissue. The streak-formed shadows may thus be a more outstanding feature than the patchy ones in early cases of pulmonary edema (case 2). After the death the lungs of this patient were photographed as a lung preparation. The roentgenogram showed a markedly increased involvement at the same time as the individual patches had become larger and more poorly defined. The patchy distribution is a typical feature in the roentgenogram in cases of fully developed pulmonary edema. This also applies to the microscopical picture. Under the low power a patchy transudation is seen scattered throughout an otherwise normal air-containing lung tissue.

It is strange that the clinical symptoms were so sparse in the presence of pulmonary edema. Except for the cyanosis and the dyspnea, none of the cases had much expectoration, nor was there pinkish forthy fluid

pouring from mouth or nose. Auscultation revealed only slight crepitant râles, not more than commonly found in bedridden patients.

The clinical picture of acute pulmonary edema is described as being characterized by a sudden onset of marked dyspnea and cyanosis associated with a rapid and shallow respiration with movement of the alae nasae. The patient is in great distress, feeling as being choked. Tracheal and pulmonary râles are heard without a stethoscope, and there is a short cough with large quantities of thin, serous, frothy blood-stained, or pinkish sputum. The pulse is rapid and tense, the skin cool and clammy. There is no definite dullness over the lungs, and beside the diminished respiration, fine crepitant and coarse, moist râles may be heard.

The chronic pulmonary edema most commonly develops in patients with heart failure. There is an evenly increasing dyspnea and cyanosis, and increasing crepitant râles in the basal parts of the lungs.

In our cases the sparse clinical findings stand in a marked contrast to the roentgenological as well as to the pathological-anatomical changes. Especially is this so as to the third case. The roentgenological changes are seen to appear before a clinical diagnosis can be made. Both ROUBIER, LELONG & BERNARD, and WERKENTHIN have called attention to this, not only seen in the case of chronic edema, but also in acute and subacute pulmonary edema (case 2 and 3).

There is an explanation to this circumstance. As previously mentioned, the essential feature is that the transudation first takes place in the central parts of the lung. Outside the central edematous area there will be an air-containing layer, which veils the central adventitious sounds and the changed percussion note which should be expected according to the increased density of lung tissue (as found in cases of central pneumonias).

The old clinicians were aware of the discrepancy between the sparse physical findings and the pathologico-anatomical preparation. To them there were reasons to believe that the heavy, firm edematous lungs would be an agonal or a postmortal phenomenon. As COHNHEIM said: »They do not die because they develop a pulmonary edema. The pulmonary edema develops because they die.»

Thus the aphorism of COHNHEIM may have to be revised. And it is the roentgen examination, therefore, that has brought these relatively silent edemas to our knowledge.

The central transudation can easily be reproduced. The removed heart-lung preparation was inflated with air through the trachea. Saline was then injected into the pulmonary artery on one side. The preparation was photographed at different stages. The roentgenological picture paralleled exactly those of the edematous lungs of human patients. Fig. 4 A shows that an area of ill defined patches of increased density have developed just around the hilus. In fig. 4 B the area of increased density

Fig. 4 A. Heart-lung preparation after injection of saline in the right pulmonary artery. Pressure 25 mm Hg.

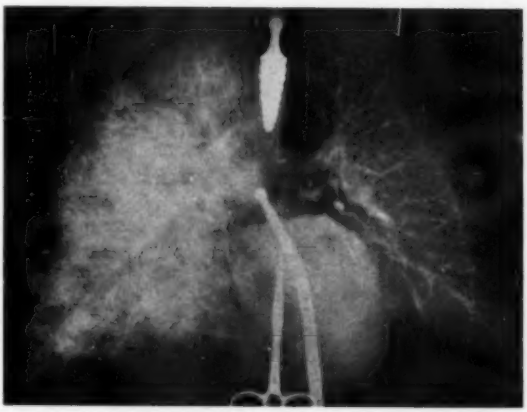


Fig. 4 B. Continuous injection of saline under pressure up to 50 mm. Hg. Note central transudation and peripheral translucency. The resemblance to fig. 3 B is striking.

has increased, and so have the individual patches. But the peripheral parts of the lung remain quite clear. The striking resemblance to the two roentgenograms 3 A and 3 B, which were taken in vivo, should be noted.

SUMMARY

Three cases of verified pulmonary edema are recorded. Clinically the patients showed remarkably little evidence of pulmonary edema. The roentgenological changes appear earlier than the clinical signs. The edema shows a central distribution, being surrounded by an air-containing layer of normal lung tissue, which explains the sparse auscultatory findings. Pulmonary edema could be produced by injection of saline into a heart-lung preparation. The roentgenological picture of the preparation corresponded to that typical of a fulminating pulmonary edema.

ZUSAMMENFASSUNG

3 Fälle von verifiziertem Lungenödem werden mitgeteilt. Die klinischen Zeichen des Lungenödems sind auffallend spärlich. Die röntgenologischen Veränderungen erscheinen früher als die klinischen Zeichen. Das röntgenologische Bild zeigt, dass die Verteilung vorzüglich central ist und dass normales lufthaltiges Lungengewebe sich wie eine Kappe das Ödem umhüllt. Hier liegt die Erklärung der spärlichen auscultatorischen Geräusche. Das Lungenödem könnte durch Injection von Kochsalzlösung in ein Herz-Lungenpräparat erzeugt werden. Das röntgenologische Bild dieses Präparats gleicht dem Bild des Lungenödem in vivo.

RÉSUMÉ

Relation de trois cas d'œdème pulmonaire qui furent vérifiés. Cliniquement les malades montraient remarquablement peu de signes de l'affection. Les modifications radiologiques apparaissent plus précocement que les symptômes cliniques. L'œdème présente une répartition centrale et est entouré de couches de tissu pulmonaire normal contenant de l'air, ce qui explique la pauvreté des constatations auscultatoires. On a pu produire un œdème pulmonaire en injectant du chlorure de sodium dans une preparation anatomique du cœur et des poumons. L'image radiologique de la preparation correspond à l'image typique d'un œdème pulmonaire in vivo.

REFERENCES

Coe, F. O. & Otell, L. S.: Acute Pulmonary Edema, Am. J. Roentgen & Rad. Therapy 1932, 27, p. 101.

Dale, T.: Der Wert der Röntgenuntersuchung in der Lungendiagnostik. Act. Rad. Suppl. 16, 1932 p. 101.

Drinker, Cecil K.: Pulmonary Edema an Inflammation. Havard University Press, Cambridge, Mass. 1945.

Graham, E. A.: Influence of Respiratory Movements on Formation of Pleural Exudates. J. Am. Med. Ass. 1921, 76, p. 784.

Kommerell, B. & Wedler, H. W.: Interstitielles Lungenödem im Röntgenbild. Fortschritte auf Geb. der Röntgenstr. 1940, 62, p. 258.

Lelong, M. & Bernard, J.: L'image radiologique de l'oedème aigu du poumon. Annales de Médicine 1937, 42 p. 624.

Nessa, C. B. & Rigler, L. G.: Roentgenologic Manifestations of Pulmonary Edema. Radiology 1941, 37, p. 35.

Rendich, R. A., Levy, A. H. & Cove, A. M.: Pulmonary Manifestations of Azotemia. Am. J. of Roentgen & Rad. Ther. 1941, 46, p. 802.

Roesler, H.: Clinical Roentgenology of the Cardiovascular System. Springfield 1946, p. 153.

Roubier: »Azotemic lungs» cit. Radiology 1939 I.

Werkenthin, M.: The Roentgenologic Aspect of Lung Edema. Am. J. of Roentgen & Rad. Therap. 1939, 41, p. 183.

Zdansky, E.: Beiträge zur Kenntnis der kardialen Lungenstauung auf Grund Röntgenologischer, klinischer und anatomischer Untersuchungen. Wiener Arch. f. Inn. Med. 1929, 18, p. 461.

Zdansky, E.: Über das Röntgenbild des Lungenödems, gleichzeitig ein Beitrag zur Frage der Pathogenese des Lungenödems. Röntgenpraxis 1933, 5, p. 248.